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THE INFLUENCE OF COMPLICATING DISEASES UPON LEUKÆMIA.*

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Investigations in leukæmia during the last decade have led to a great increase in our knowledge of the phenomena of that disease, especially of the minute changes in the blood and tissues. But the gains hitherto have added complexity to the subject by suggesting new problems, instead of clearing up the old ones. Failing the discovery of some microscopic germ as the cause from which the various changes can be traced, the elucidation of many details is likely to be brought about only by patient labor in piling up and analyzing observations.

With this idea I have examined one interesting feature, perhaps I should say one set of features in the disease, viz., the changes following or associated with intercurrent disease. Cases of this kind are rapidly multiplying in the literature, and, having had some instructive cases of my own, it seemed to me that a study of these and others might be useful. I soon found that the outcome would not be as rich as I hoped, but the subject seemed worthy of presentation on account of the nature of the material now available.

I will cite my most important case, leaving out many details of the history:

Case I. *Myelogenous (mixed-celled) leukæmia; influenza; reduction of leukocytes to* 5000 *and below; gradual rise of leukocytes six weeks after the complication, reaching* 157,000 *in another month;*

* Read before the Academy of Medicine of Cleveland, September 18, 1903.

death seventeen months after the complication.—Mrs. C. D. A., aged forty-two years, housewife, was first seen December 29, 1896. From the notes made then I quote: Patient complains of swelling in the left side, shortness of breath, and weakness. The family history is negative as regards ancestors. The husband, who seemed well during the patient's lifetime, developed splenic anæmia a year after her death. (See *Transactions of Association of American Physicians*, 1903.) The daughter, after the mother's death, had lymphoid hyperplasia in the pharynx and tongue and in the appendix. The latter was the seat of frequent and severe pain; it could be felt as a hard body, as thick as a lead-pencil, through the strong and well-nourished abdominal wall, and was removed at my advice and found to be free from evidences of inflammation, but with lymphoid tissue unusually developed.

Besides the usual acute infectious diseases, the patient had ague twice in childhood, but does not think she had enlarged spleen, "ague-cake" being a familiar sign in that vicinity at the time.

Menstruation began at thirteen years, and was always regular, except during pregnancy, up to two years ago. Since then the flow has been greater, but pale, and accompanied by bearing-down pains.

At nineteen years she had "dysentery," passing blood with the stools for one month. A series of furuncles on the arms and back followed this. She was then fairly well for ten years, was married, and, except for an abortion after the first pregnancy, remained well until her second and last pregnancy, eight years ago. About the fifth month she had a pain in the abdomen, back, and right shoulder, which closely resembled biliary colic. The patient ascribes all her trouble, however, to the confinement, which was difficult, but the exact results of which do not appear. Three months after it she became intensely jaundiced, and remained so for two weeks. The abdominal pain mentioned above returned then, and at intervals, but without jaundice, up to two years ago.

Two years ago the patient thinks the present disease began, with chilly feelings in the back and hands. In two days there was pain in the splenic region, sore throat, pain in the extremities, and slight fever. The chills lasted for two months, occurring sometimes twice a day, followed by fever and sweating. The pain in the left side continued up to six weeks ago. It was thought to be pleuritic. Three months ago the swelling on the left side was discovered by the patient. It was then about the size of an apple. Soon after the swelling was discovered the chills and fever returned, with paroxysms, usually about 11 A.M. and 2 or 3 P.M., but any exertion was likely to be followed by a chill. The tumor gradually became larger. About two months ago a throbbing pain began in the posterior part of it, and lasted about a month. Then severe and unexplained vomiting came on, and in a paroxysm of vomiting it seemed as if something had fallen in the splenic region. Since then the pain

has been less severe. Shortness of breath on exertion has increased gradually in the last year. There have been no hemorrhages. Headache has been troublesome for some months.

Status præsens, December 29, 1896. Patient is of small size, medium frame, muscles and panniculus well nourished. The superficial lymphatic glands are not enlarged. The face and visible mucous membranes are of good color, but the hands are pale.

The thorax is symmetrical in the upper part. Examination of the lungs negative.

The heart is in the normal position; dulness not enlarged. There is a soft systolic murmur all over the heart area; the first sound is loud. Radial pulse small, quick, regular.

The abdomen is large, especially in the left upper part, where the thorax is also fuller. The recti are separated. The lower edge of the liver is almost at the navel line, but deep in the abdomen. The edge is thin and tender on pressure.

The splenic dulness begins in the seventh interspace and extends down into the mass below the ribs, evidently the spleen, which can be easily felt as a flattened body reaching to the level of the anterior superior spine of the ilium and to the median line. The edge is thick; there is a shallow notch on the inner side. There is palpable and audible friction over the surface. The patient says the mass is sometimes lower than at present. It is not unusually movable by pressure or position.

There is pain on pressure over the sternum and tibiæ.

The blood is pale, not very thin; fresh preparations show enormous increase of the leukocytes, among which large cells with fine or coarse granules are conspicuous. The blood count shows: red corpuscles, 2,500,000; leukocytes, 367,070; hæmoglobin (Fleischl), 50. Stained preparations show moderate poikilocytosis, many nucleated reds—1: 40 leukocytes, or 9074 per c.mm. About one-fourth have the size and appearance of megaloblasts, but the two forms run into each other by variations impossible to classify precisely. Differential count of the leukocytes shows: lymphocytes, 0.3; mononuclear neutrophiles, 48.8; polynuclear neutrophiles, 41.6; polynuclear eosinophiles, 0.7; mononuclear eosinophiles, 1.4; basophiles, 2; degenerated, 5. The lymphocytes are often smaller than red corpuscles, but do not show as intense staining of the nucleus as do typical small lymphocytes, and have usually a distinct rim of protoplasm. Many of the myelocytes have deeply indented nuclei, but the looser, skein-like structure of the nucleus distinguishes most of them from those denominated polynuclear. The eosinophiles, especially the mononuclears, vary much in size from that of a small lymphocyte to that of the largest mononuclears. The basophile cells are large or small in about equal proportions. The degenerated leukocytes are hard to classify, but seem to represent all the larger forms.

The diagnosis of myelogenous, mixed-celled leukæmia was given, the usual prognosis stated to the husband, and Fowler's solution recommended to the family physician.

February 1, 1897. The patient entered the medical clinic of the University Hospital. She says that two weeks ago she had influenza, with tonsillitis and coryza. The discharge was bloody, especially in the morning, and a week ago there was moderate nose-bleed. She complains now of great weakness, dyspnœa, pain in the left side, and general itching. She "feels as if walking on sticks."

Status præsens. The patient looks somewhat more anxious than before. The skin is not very pale. The hands feel numb when the arms are fully extended. There is no distinct tenderness over the nerve trunks of the extremities. The tongue is clean. There are no stomach symptoms. The pharynx shows moderate redness and swelling, with scanty mucopurulent exudate. The thoracic organs are negative, aside from a few small rales in both bases on deep inspiration, and a soft systolic murmur over the base of the heart. The abdomen is above the level of the ribs. The edge of the liver is within an inch of the navel line. The spleen extends three fingers' breadth below the margin of the ribs. The lower end is rounded, a shallow notch can be felt just above the point. The spleen is very tender on pressure, freely movable. There is distinct friction over it. The superficial lymphatic glands are not enlarged. There is no œdema of the ankles. The blood count: red corpuscles, 2,540,050; leukocytes, 7500; Fleischl, 50 per cent. Red corpuscles show marked vacuole formation; many polychromatophiles; some red corpuscles show mitotic figures. The arsenic had been increased up to 12 drops t. i. d.; it was continued, with extract of red bone-marrow (4 c.c. t. i. d.).

February 2*d.* Red corpuscles, 2,500,000; leukocytes, 8125; Fleischl, 50 per cent. Differential counts given in table.

7*th.* Patient complains of more numbness and also of itching. Arsenic stopped. Temperature has been up to 101° to 101.6° F.; pulse, 110; respiration, 22.

9*th.* Red corpuscles, 2,192,000; leukocytes, 4775; hæmoglobin, 50 per cent. Temperature has not been higher than 99.4° F.; pulse, 80 to 100; respiration, 22. Patient still complains of itching, also of weakness, headache, and slight dizziness.

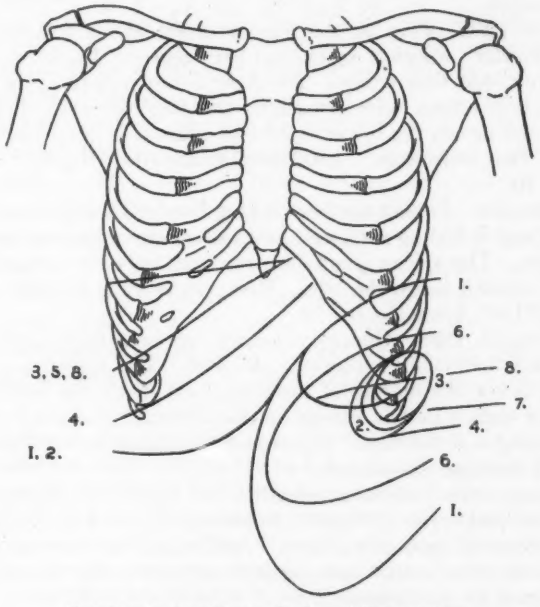
12*th.* Red corpuscles, 2,863,000; leukocytes, 5000. The condition remained about the same. The temperature was rarely above normal; there was slight gain in weight. Itching was the most troublesome symptom.

March 3*d.* The leukocytes number 35,156; red corpuscles, 3,733,333; hæmoglobin, 60. The spleen can barely be felt on quiet breathing. On deep inspiration it extends three fingers' breadth below the ribs. Splenic dulness begins on the ninth rib and is 9 cm. long. On the right side there is dulness from the sixth intercostal

space to an inch above the margin of the ribs and to the tip of the ensiform. The abdomen is slightly distended; no enlarged glands can be felt in it. The inguinal glands are slightly enlarged.

10*th*. Red corpuscles, 3,125,000; leukocytes, 40,170; hæmoglobin, 55. The systolic murmur over the base is still present. There is no œdema.

21*st*. Red corpuscles, 3,100,000; leukocytes, 90,000; hæmoglobin, 70. The patient feels better than before. Has no subjective symptoms. The spleen can barely be felt on quiet breathing; liver not enlarged. Patient has gained eight pounds in all since admission.



Variations in size of liver and spleen at different stages.

April 2*d*. Red corpuscles, 3,281,200; leukocytes, 157,000.

5*th*. Patient is going home. Feels very well. Spleen and liver as at last note. Red corpuscles, 3,580,000; leukocytes, 189,000. Continues Fowler's solution.

15*th*. Red corpuscles, 3,825,000; leukocytes, 217,600. No subjective symptoms; spleen as before; slight œdema of feet.

June 4*th*. Red corpuscles, 3,600,000; leukocytes, 307,000. Next day, at home, patient had a chill, followed by several others in the next twenty-four hours, and for the next three weeks had a good deal of fever. Severe pain in the splenic region required the use of morphine for sixteen days.

July 1*st*. Red corpuscles, 3,600,000; leukocytes, 307,000. The patient feels as well as before the febrile attack. She has tingling in the toes and fingers; otherwise well. She has gained eight pounds since leaving the hospital. The spleen is three fingers' breadth below the margin of the ribs on quiet breathing; it is hard and thicker than before. The liver is three fingers' breadth below the ribs, the edge thin and of normal consistency. Fowler's solution, stopped during the fever, renewed.

22*d*. Feels better. Took Fowler's solution up to 10 drops. The hands are better; the feet tingle slightly. Red corpuscles, 3,600,000; leukocytes, 178,000. The spleen is slightly smaller. Is now taking bone-marrow.

August 19*th*. Pain in the legs returned about ten days ago. Began Fowler's solution again, and pain ceased. Looks well; does housework, but tires easily. The liver is not palpable; the spleen is much larger than before, reaching two finger-breadths below the level of the navel; the upper border of dulness in the eighth interspace. Red corpuscles, 4,000,000; leukocytes, 165,000; hæmoglobin, 70.

October 21*st*. Patient has been taking Fowler's solution and bone-marrow and is feeling well, and now looks better than she has for a long time. The spleen is smaller, reaching only two and one-half fingers' breadth below the ribs. Red corpuscles, 4,000,000; leukocytes, 57,000; hæmoglobin, 70.

January 27, 1898. General condition has been fairly good. Red corpuscles, 3,095,000; leukocytes, 461,666. The spleen is a hand-breadth below the margin of the ribs, 3 cm. from the middle line. The liver cannot be felt, except on deep breathing; there is dulness to the margin of the ribs. The superficial glands are not enlarged. Fowler's solution continued.

February 26*th*. General condition is good. Red corpuscles, 3,533,333; leukocytes, 279,260. Spleen as at last note. This was the last time the patient was seen. April 17th she wrote to say that she was not able to travel, on account of pain in the abdomen and enlargement of the spleen.

June 8*th*. Reported that patient, who had been trying to come to the hospital, had fever, chills, nausea, and vomiting, and was very weak. "The spleen fills the entire abdomen."

17*th*. "Patient is able to sit up, but still very weak. Is entirely deaf and complains of roaring in the ears." Soon after this she died, while I was away from home. An autopsy was made, but no tissues preserved.

Summary of the case: A woman with mixed-celled leukæmia, with greatly enlarged spleen. Two weeks after an attack of what was probably influenza, the leukocytes were found reduced from 367,070 to 7500, falling to 4775 in two weeks more, with reduction, but not disappearance, of the abnormal white and red cells. The

spleen was much smaller; the liver became smaller later. In two months from the complication the leukocytes reached 40,000, in ten weeks 157,000, and in a year 461,666, having once been as low as 57,000 in the mean time. The liver and spleen remained small for many months, though the spleen was usually easily palpable. For the next six months the patient grew worse in every respect, and died a year and a half after the first observation. The most important stages in the blood are shown in the following table:

Date.	Red cells.	White cells.	Hæmoglobin.	Nucleated red cells.	Small lymphocytes.	Large lymphocytes.	Transition and large mononuclear.	Polynuclear neutrophiles.	Polynuclear eosinophiles.	Mononuclear eosinophiles.	Myelocytes (Ehrlich).	Basophile.	Degenerated.
Dec. 29	2,500,000	367,070	50	9074	0.00	0.30	00.0	41.6	0.7	1.4	48.8	2.0	5.0
Feb. 1	2,541,050	7,500	50										
" 2	2,500,000	8,125	50	2358	4.2	5.7	4.9	70.6	.....	.....	12.3	.....	6.0
" 9	2,192,000	4,775	50	1224	2.5	11.8	10.1	56.0	.....	1.4	11.1	1.0	6.0
" 12	2,868,000	5,000	...	416	1.6	13.3	3.3	63.8	0.3	0.6	9.6	1.0	6.6
March 3	3,733,333	35,156	60	524	0.4	7.6	7.1	66.2	0.2	.....	15.5	.....	2.7
" 10	3,125,000	40,170	55	362	0.15	5.2	2.4	54.4	.....	.....	20.9	.....	16.4
" 14	3,125,000	40,170	50	500	0.8	2.4	1.4	62.0	.....	0.2	29.9	.....	3.3
" 21	3,100,000	90,000	50	few	0.1	2.3	3.2	63.7	0.4	0.2	22.3	.....	6.4
Oct. 21	4,000,000	57,000	70	1760	1.3	3.5	7.7	62.0	1.2	1.3	20.8	0.9	2.3
Jan. 27	3,095,000	461,666	65	7387	2.3	1.3	4.4	63.2	0.4	0.7	27.0	.....	0.7
Feb. 26	3,533,333	279,000	70	6700	3.8	6.0	3.0	41.0	1.0	0.3	34.0	1.0	5.0

Such a change, more marked than one usually sees in leukæmia under treatment, forces one to try to learn something from it, not only as regards pathology, but, even more imperatively, something of therapeutic value. The most important objective symptom, the excess of leukocytes, disappears. It would seem that by examining such cases one might discover something regarding the production of leukocytes and their appearance in the circulation, as well as their ultimate destruction; also something of the life of the red corpuscles, and of other details of the pathology of leukæmia. It might seem that the process could be imitated, and a symptomatic, if not a causal, treatment be discovered. Medical literature contains a number of such cases, though not so many as one might expect, remembering the vulnerability of the leukæmic to infection. Not only single cases have been reported, but studies have been made, and in the present article I am merely going over ground that has already been traversed by others, my only advantage being due to the fact that I am at present the latest inquirer.

The literature of the complications is unusually confused. Some of the cases have been reported two or even three times by the same

or different authors. Besides unavoidable errors, such as those in ages, dates, and other minor details, author's names have been changed. H. Strangways Hounsell, one of the earliest authors, becomes Honsell, Hantell, Strongways, Srangways, and even, by an unnecessary comma, two authors, contributing a case each. Thorsch reported a case in his own name, from the clinic of von Limbeck, and at least two writers ascribe it to "Zeissl," whose name does not appear in the original article.

The subject is complicated by other things. A frequent cause is the lack of exact classification of the leukæmia. In many cases I have been obliged to follow the author's terminology and classify cases that should, perhaps, be otherwise arranged. With future cases this difficulty will become less frequent, and also another regarding the diagnosis of the complication. But owing to the chronic and obscure course of many cases and the tendency of patients to wander from one to another physician, incomplete observations will multiply, and will, nevertheless, often deserve publication.

I shall discuss the cases according to the nature of the complicating disease in the first place, and the variety of leukæmia in the second, and, without trying to follow a scientific order, will speak first of tuberculosis.*

Cases of Tuberculosis and Leukæmia.

The combination of tuberculosis and leukæmia was noted very early. Virchow[1] described a case in 1849, and his rival, Bennett,[2] noted 2 out of 23 cases collected in 1852. Virchow also made the anatomical examination in a case observed clinically by Bamberger[3] in 1857. According to Mosler,[4] there were 12 examples of tuberculosis in the 100 cases of leukæmia analyzed in Martin Ehrlich's thesis in 1872. Yet in the recent literature the combination is rarely mentioned. Many authors admit that they have never seen such a case. It was encountered only twice in the 37 cases observed in the Göttingen clinic,[17] with 10 autopsies. Among my own cases, 25 in number, there were no clinical evidences, but in 2 out of 6 autopsies miliary tuberculosis was found, once in a marked degree. I think that more extensive observations will show that the exclusion is not so absolute as has been thought. In my own clinical material leukæmia occurs most frequently in the early part of the fifth decade, when tuberculosis is relatively infrequent. Cornet, Moorehouse, and others have pointed out that this age period is one very prone

* Three articles were received too late to use in this paper. Tommaso Prodi, La Riforma Medica, July 22, 1903, A Case of Lymphatic Leukæmia, with Tuberculosis of the Larynx, Lungs, and Lymphatic Glands. W. J. Susmann, The Practitioner, October, 1903, Tuberculosis in One out of Forty-one Cases of Leukæmia Observed in Various London Hospitals. Wilhelm Neutra, Zeitschrift f. Heilkunde, Band xxiv., 1903, Two Cases of Lymphocythæmia; in one Pleurisy, with Leukocytes Dropping from 160,000 to 8800; in the other, Suppurative Pleurisy and Peritonitis; Blood Not Thoroughly Examined.

to tuberculous manifestations, but I think the whole subject is one that requires further investigation. This is one of many aspects of leukæmia that can be studied with advantage by the physician in private practice, where the whole course of the disease can be followed. Owing to the nature of the disease patients with leukæmia do not remain in hospitals as long as is desirable for extensive study.

Another fact requires some consideration. Small leukæmic growths closely resemble tubercles. The early literature has occasional mention of leukæmic growths, sometimes of large masses that, especially in the lungs, break down and simulate ulcerative tuberculosis. At an early period Virchow, Boettcher, and Ollivier and Ranvier studied the peculiarities of the two growths, but it was not until the structure of tubercle had been more minutely described by Wagner, Schüppel, and Langhans, and especially after the discovery of the tubercle bacillus, that the differentiation was made certain. It would be interesting to re-examine some of the old museum preparations with reference to the breaking down of such growths. The analysis of cases published before 1882 is very unsatisfactory. The only cases necessary or profitable to examine now are those in which an effect on the blood or organs has been noted.

There are in the literature about 27 cases that either are cited in this connection or might be referred to. To these I add two imperfect observations not previously reported. The cases of Virchow and Bamberger, mentioned above, throw no light on the question now under consideration. That of Hounsell,[5] fairly well described, is of value also only in showing the association of diseases. Besides tuberculosis the patient had scarlet fever, tonsillitis, and secondary pneumonia. The leukæmia was probably acute lymphocythæmia. Ollivier and Ranvier[6] reported the case of a man, aged forty years, with miliary tuberculosis of the abdominal organs, old pulmonary tuberculosis, and leukæmia. The case cannot be analyzed for lack of details regarding the blood. The same difficulty exists in the report by Robin[7] of a case of extensive lymphatic tuberculosis with leukæmia. Still less available is a case mentioned by de Roth,[8] of miliary tuberculosis and leukæmia, observed by Knoepfelmacher, but not published. Brueckmann[9] has reported a case of splenic-myelogenous and lymphatic leukæmia with old and recent tubercles that has some incidental interest, because it appears that the examination of the blood made in a famous German clinic, in 1892, consisted in estimating the proportion of red and white cells in blood, "mit Wasser stark verdünnt." Two cases reported by Volpe[10] are even more imperfectly described, and do not add anything to the material, while several of 6 cases he quotes from the literature are cases of pseudoleukæmia. In a case of Musser and Sailer[11] there were "evidences of old tubercle" in the apex of one lung. This and a similar case reported briefly by Saundby[12] show that leukæmia can develop in bodies with old tuberculous foci, as is proved by some

of the cases cited below. Sabrazès[13] has briefly mentioned a case of myelogenous leukæmia and tuberculosis of the lymph glands, with diminution of eosinophiles and mast-cells, and increased polynuclears. The patient reported by Strattmann[68] had a history of apical catarrh and pulmonary hemorrhages before the spleen became large, and may also have been tuberculous. The patient treated with tuberculin by H. Heuck,[64] mentioned below, also had slight signs of pulmonary tuberculosis.

Finally, in Kraus'[32] case, discussed below, there was miliary tuberculosis besides the streptococcus and diplococcus infections.

Of the other 15 cases 7 are examples of medullary leukæmia, with acute miliary tuberculosis. Of these, the cases of Quincke [14 15] (2 cases), Lichtheim,[16] Schmidt,[17] Bezançon and Weil,[18] and Hirschfeld and Tobias[19] showed diminution of leukocytes as follows:

Quincke, Case 1	1 : 3	to	1 : 50
Quincke, Case 2	1 : 4	to	1 : 90
Lichtheim*	1 : 8	to	1 : 370 (250,000 to 8,900)
Schmidt	1 : 2.9	to	1 : 135 (962,000 to 28,000)
Bezançon and Weil	135,000	to	19,871, rising to 45,000
Hirschfeld and Tobias	331,000	to	110,937

In Schmidt's case there were small cavities in the lungs. In Hirschfeld and Tobias' case there were old lesions in the apices, but not cavities, and no clinical symptoms of tuberculosis. The miliary tuberculosis does not seem to have been very severe. No bacilli were found in sections. The leukocytes were as high as 434,000 nine months before the low count, 228,000 four months before, rising to 331,000 two weeks before the low count. Six months later, after a recurring pneumonia, they numbered 283,333, and death occurred five weeks later. In the case of de Roth[8] there was a rise toward the end.

Four cases of myelogenous leukæmia are recorded in which chronic tuberculosis existed, sometimes ending in miliary tuberculosis. These are reported by Elsner and Groat,[20] Sturmdorf,[21] Parker,[22] and Murrell,[23] though the tuberculosis in the latter case may not have been very chronic. In all there was a fall in the number of leukocytes toward the end. In some the lowest count was still so high as to leave little room for doubt as to the diagnosis, viz., in Elsner and Groat's case, 121,000; Sturmdorf's 116,000; Parker's, 100,000, later 130,000; but in Murrell's it was 16,200, from 220,000. Arsenic was freely used in this case.

The other cases show variations in the leukæmic condition and other features that make it necessary to consider them separately.

In the case of Stintzing[24] there was enlargement of the spleen and lymphatic glands, with old tuberculous lesions (cavities) in the

* Elsner and Groat and Hirschfeld and Tobias classify Lichtheim's case among lymphatic leukæmias, but as the author says the polynuclear and mononuclear cells were about equal, I agree with Baldwin and Wilder and Quincke in placing it with the splenomedullary cases, though the lymph glands were also enlarged.

lungs. The leukocytes decreased slightly, 1:100 to 1:150; the glands became smaller, but the spleen remained about the same size. It is difficult to understand the author's statement that the "leukæmia improved while the phthisis made great progress," particularly as the patient died, unless we take a very partial view of the case.

Juenger's[25] patient had enlarged lymphatic glands, and probably acute leukæmia, though the description of the blood leaves some doubt as to its precise character. Miliary tuberculosis of the glands and peritoneum, with early caseation, was found post-mortem. The leukocytes rose from 40,000 to 125,000 in two weeks, two and a half months before death, and fell to 68,800 six weeks before the end, following an attack of diarrhœa. Arsenical pigmentation was then present. The glands became smaller. An abscess in one of them was incised. The blood was not examined again until two days before death, and then showed no excess of leukocytes.

In Francksen's[26] case, probably also lymphatic leukæmia, there was tuberculosis of the lymph glands, spleen, and liver, with final bronchopneumonia. The leukocytes fell from 240,000 to 128,000 between observations four months apart, and did not fall lower in the next three days, or two days before death. The spleen became smaller toward the end.

Baldwin and Wilder[27] reported a case of probable chronic lymphocythæmia. In this lymphatic enlargement had lasted more than two years, chronic pulmonary tuberculosis, finally developing cavities, as long or perhaps longer. The leukæmia was observed for about two months. There were no recent miliary tubercles. The leukocytes numbered 695,000 at the beginning of the period, reached 1,113,000 nine days before the last count, and then fell to 943,500 and 959,500, without qualitative changes. The lymph glands and spleen grew smaller four days before the end.

From the available material it appears that chronic tuberculosis does not distinctly influence the course of leukæmia, or, as we shall see later, materially influence the leukocyte formula. Acute miliary tuberculosis, on the other hand, is followed by or associated with reduction of the leukocytes in the majority of cases. The exceptional cases may be due to the slight development of the miliary tuberculosis in extent, or to the fact that death occurs before the change has time to take place, though it may be, as de Roth has suggested, that in some cases the body becomes accustomed to the infection and the leukocytes are not affected, as in more acute cases.

Two of my cases, though imperfectly observed, add weight to both of the first two suppositions.

Case II.—M. T., domestic, aged twenty-five years, first seen June 2, 1896. "She was well until July, 1895, when swellings and red spots appeared on the right leg, and similar lesions appeared on various parts of the body up to the time of examination. The abdo-

men has been large for nearly a year. It was supposed to be due to uterine or ovarian tumor, for which an operation was advised by two physicians she consulted. Weakness present for three months." I found a mixed-celled leukæmia, with red corpuscles, 3,587,500; leukocytes, 598,000; hæmoglobin, 60. There were ecchymoses, up to the size of the palms, on the arms and legs. The spleen extended one inch beyond the middle line, and to the level of the anterior superior spine of the ilium. The liver was not enlarged; the axillary and cervical lymph glands were slightly enlarged, but not the inguinal glands. No pain or tenderness in the bones.

The patient was observed by Dr. Cowie and myself for two years, taking Fowler's solution as steadily as is usually possible. Within three weeks the ecchymosis ceased, menstruation reappeared after an absence of several months, but there was no marked fall in the leukocytes and no noteworthy change in the leukocyte formula. Myelocytes varied from 25 per cent. to 44 per cent.; polynuclears, 30 per cent. to 50 per cent.; lymphocytes, 1 per cent. to 6 per cent.; polynuclear eosinophiles, 1 per cent. to 3.2 per cent.; mononuclear eosinophiles, 1.2 per cent. to 1.8 per cent.

Becoming anxious for more radical treatment, the patient disappeared from our observation. A year later, three years after the first observation, Dr. Cowie and Dr. Warthin were given an opportunity of making an autopsy by the courtesy of Dr. J. A. Wessinger, who had been called upon in the last illness. The spleen was enlarged; the chief picture was that of a severe tuberculosis of the serous membranes. The blood showed no increase of leukocytes, and microscopic examination of the tissues revealed a complete absence of leukæmic changes, except in the bone-marrow, which was lymphoid.

In this case it is impossible to know when the change occurred. The tuberculosis was more severe than it seems to have been in many of the reported cases.

In Case III., to be reported more fully on account of other features, a man, aged twenty-nine years, died with so-called leukæmic apoplexy, without any decrease of leukocytes up to the moment of death. At the autopsy a slight recent miliary tuberculosis was found. Striking as the differences are in these two cases, I think we should await the publication of others before drawing conclusions from them.

Miscellaneous Infections.

There are 23 reported cases of intercurrent infection other than tuberculosis, including my own Case I. The infections represented are: In medullary or splenomedullary leukæmia: typhoid-like disease (Eisenlohr[28]), afebrile typhoid (Pal[29]), erysipelas (Richter[30]), also reported by Freudenstein;[31] erysipelas, streptococcus, and diplococcus infection with miliary tuberculosis (Kraus[32]), sepsis (H. F.

Mueller,[33] Koermoeczi[34]), empyema (G. Heuck[35]), influenza (Kovacs,[36] Dock), peritonitis (Da Costa[37]).

In lymphatic leukæmia, acute in most cases: sepsis, angina (H. F. Mueller[38]), angina, streptococcus (Weil[39]), streptococcus infection (Wende[40]), sepsis (Cabot[41]), staphylococcus (Fraenkel[42]), colon bacillus (Fraenkel, *ibid.*), staphylococcus and colon (E. Mueller[43]), pneumonia (Oette,[44] Froelich,[45] Thorsch[46]).

Chronic lymphocythæmia was observed complicated by pneumonia by Grawitz[47] and Hart,[48] and bronchitis by Petit and Weil.[49] In some of the cases more than one complication was observed, and these I shall utilize as far as the data will perm .

The following may also be mentioned: Heusner, in discussing Strattmann's case,[68] mentioned a patient with leukæmia in which diminution in the size of the glands and spleen and improvement of the blood followed pneumonia, but relapsed. Rieder[50] (p. 38) has reported a case of medullary leukæmia with sepsis, and one of lymphatic leukæmia and sepsis, with increase of the leukocytes. The details are too scanty to use. The case reported from Mosler's clinic by Oette[44] may be mentioned here, though I might have included it among the more important cases. A girl aged twenty-three had fever with icterus. The leukæmic blood improved after six weeks, and six months later was "almost normal." The case is of great historical interest, and Oette's thesis of much value, but the case cannot now be compared with others. Chantemesse, in the discussion of Bezançon and Weil's case,[18] mentioned a patient of his who acquired erysipelas in the course of leukæmia.

Of the cases referred to above, there was a marked decrease of leukocytes to or near normal in 11, viz., those of Eisenlohr, Kraus, Wende, Froelich, Fraenkel (2 cases), Oette, Koermoeczi, Dock, E. Mueller, Cabot. There was a relatively slight fall in 9, viz., those of Pal, Richter, H. F. Mueller, Weil, Thorsch, G. Heuck, Kovacs, Hart, Grawitz. No change or a rise in 3, viz., Mueller, Petit and Weil, Da Costa.

The cases differ so much in detail that it is difficult to make comparisons. Taking first streptococcus infections, we find that in Richter's case of facial erysipelas following puncture of the tympanic membrane, the leukocytes had fallen on the second day of the complication to 56,000 from the 320,000 of two weeks earlier. The spleen was smaller, and in three days more was 4 cm. less in length, 3 cm. in width. The leukocytes sank to 29,000 on the fourth day, but rose rapidly to 148,000 on the sixth day, along with the development of an abscess of the eyelid and bronchitis, and fell to 52,000 in six more days, while the general and local conditions improved.

In Weil's case of angina with streptococci in the blood, the leukocytes fell during blood infection from 290,400 to 75,682 in four days; seven days later, 66,230. The author thought the angina had in-

creased the leukocytes (the blood had not been examined before), which he estimated at 60,000 to 80,000. I can see no ground for this assumption.

In Kraus' case there was in the beginning a leukocyte count of from 360,000 to 420,000. The complication, a streptococcus and diplococcus infection of the bronchi with miliary tuberculosis, ran a somewhat obscure course, the blood symptoms being the only marked ones. After slight physical signs of bronchitis, blood-streaked sputum appeared, with fever and increased size of the spleen. The leukocytes were then 393,400, but fell to 251,600 in about seven weeks, during which there was erysipelas. Two weeks later the count was 240,000. In three weeks they numbered 390,000, in four weeks 504,000. The bloody sputum then contained the cocci mentioned. The sputum then ceased; there were no signs of pneumonia. In three days the leukocytes fell to 120,000, in eight days more to 4600, without myelocytes, mononuclear eosinophiles, mast-cells, and nucleated reds, but with many degenerated leukocytes. The spleen became smaller in the next few days. The leukocytes rose to 9000; death followed four days after the last count. Autopsy revealed pneumococci in the purulent exudate in the peritoneum and in the spleen and liver, bilateral pneumonia, purulent pleural exudates, pylephlebitis, and tuberculosis of bronchial glands, lung, larynx, peritoneum, and liver. The anatomical diagnosis of leukæmia could not be made. What part the various infections played is difficult to say, but the streptococci do not seem to have been so much concerned as the diplococci. The tuberculosis was probably too slight to be effective.

In one of Pal's cases of medullary leukæmia with bronchitis and erysipelas the leukocytes rose from 75,000 to 105,000 in two days Tracheotomy was necessary, and death occurred a week later.

In Wende's case, lymphatic leukæmia with streptococcus infection, there was a marked fall, 45,000 to 600.

In Thorsch's case of pneumonia in lymphatic leukæmia (also cited by von Limbeck[51] and sometimes referred to as Zeissl's case) there was a rapid fall in the beginning from 119,000 to 43,500 by the fifth day. Next day there was an extension of the disease, and in three days more the leukocytes rose to 172,000 on the morning of the day of death, 133,000 in the afternoon.

Froelich's case was probably one of lymphatic leukæmia, though the author called it pseudoleukæmia. Under complicating pleuro-pneumonia the leukocytes fell from 66,667 (having been 309,000) to 8823 in the last week.

In Oette's case of chronic pneumonia the data are insufficient for analysis. He mentions two cases from the older literature showing that bronchopneumonia does not always alter the blood picture in leukæmia, as it had in his own case.

In chronic lymphocythæmia 2 cases have been reported compli-

cated by pneumonia. In that of Grawitz the leukocytes, "already rather low," sank lower in the beginning and rose to a considerable height in defervescence. There was no change in the formula.

In Hart's case there was a fall of from 1,168,000 to 450,000 on the fourth day of pneumonia. Death occurred two days later.

The 2 cases of influenza cannot be compared with accuracy, because in 1, my own, the diagnosis was based on the anamnesis only. In Kovacs' case the leukocytes, only 67,000 at the highest count, though they had been higher, apparently, fell to 17,000 eleven days later. Six days later there were 33,000. The patient also had bronchitis, pneumonia, and otitis. In one of H. F. Mueller's cases the patient gave a history of influenza, not observed by the author, with diminution in the size of the enlarged glands, which regained the original size after the fever subsided.

The various cases reported as examples of sepsis complicating leukæmia cannot be compared with advantage, but some of them have points of interest that deserve mention. One of the first was the case of H. F. Mueller.[38] A man with lymphatic leukæmia, with 180,000 leukocytes, had a subperiosteal abscess in the right leg. A count made then, three weeks after the former one, showed 400,000 leukocytes. The glands were about a third their former size; the spleen was also smaller. Death ensued four days after the last count. In Cabot's case of sepsis in lymphatic leukæmia there was a sudden fall from 40,000 to 5661 in one week, and a progressive fall to 471 in nine days more. In Koermoeczi's case of myelogenous leukæmia with sepsis, originating in the nose and leading to hemorrhagic pericarditis without bacteriæmia, the leukocytes fell from 100,000 to 2000. In H. F. Mueller's case of myelogenous leukæmia there was sepsis following abscess from therapeutic injections. The leukocytes had already fallen from 406,200 to 246,900, influenza having been passed through. They then fell to 225,000 with the onset of sepsis, and in the following seven weeks reached 75,500. Pleurisy and pneumonia then developed, and ante-mortem, eighteen days after the last count given, there were 57,300 leukocytes. The spleen was smaller in the later stages; the leukæmic character of the blood was lost.

In both of Fraenkel's cases of acute lymphæmia, one of staphylococcus infection, the other colon infection, there was a marked fall from 123,000 to 600 in twelve days, and 220,000 to 1200 in sevendays.

In E. Mueller's case of acute lymphæmia with streptococci, staphylococci, and colon bacilli in the exudate in the pharynx, the leukocytes fell from 109,600 to 6800 in five days, 39,200 in the last twenty-four hours.

In Eisenlohr's case of typhoid-like infection, the leukocytes, enormously increased before, fell to almost normal. An attack of follicular angina was followed by an increase, which did not subside in the remaining four weeks of life.

In Pal's case of afebrile typhoid there was a fall from 991,000 to 650,000 in sixteen days, most of it in eight days. Death occurred a week later. Pal could not see that the typhoid infection (not suspected during life) had any influence on the blood or other clinical phenomena. Besides the typhoid there was jaundice, and a traumatic, suppurating hæmatoma.

In G. Heuck's case of empyema there was a variation of from 400,500 to 80,100, rising after thoracotomy to 169,800.

I have already mentioned H. F. Mueller's case, in which the leukocytes increased during infection. Two other similar cases have been recorded. In the case of Petit and Weil there was chronic lymphocythæmia. Bronchitis occurred, fatal on the sixth day, after diminution of the enlarged glands. The leukocytes increased in the period from two days before bronchitis to the last day from 202,238 to 398,866. Da Costa[37] mentions a case of splenomedullary leukæmia, in which, within ten days after the onset of peritonitis, the leukocytes rose from 245,000 to 400,000.

The cases just cited are of importance chiefly in a suggestion they offer. In all three the rise of leukocytes was discovered early in the complication; the patients died soon after. It is possible, of course, that a fall might have occurred after the rise had the cases ended less abruptly. The earliest period after complication has rarely been carefully observed and should be thoroughly studied in future.

From the foregoing it appears that in the great majority of cases intercurrent infections cause a decrease of the leukocytes in leukæmias of various kinds. The fall may be so slight as to leave the gross picture of leukæmia unchanged, but in about half the cases the white corpuscles fall to normal or below. It is interesting to note the extreme leukopenia that occurred in some cases: 600 in one of Fraenkel's, 1200 in another, 600 in Wende's, 471 in Cabot's, 2000 in Koermoeczi's.

Besides the leukocyte decrease, the organs, enlarged as the result of the leukæmia, became smaller. In some cases the organs became smaller later than the fall of leukocytes (Quincke[14]), sometimes earlier, in others simultaneously; sometimes the organs became smaller without diminution of leukocytes (H. F. Mueller, Petit and Weil). The diminution was sometimes very rapid. Quincke estimated the change in the volume of the spleen in one case at 100 grams a day, a loss that I think must have been exceeded in my own case. It is often difficult to distinguish between this change in the organs and that observed in some cases of leukæmia a short time before death. Sabrazès mentions a case in which cutaneous neoplasms became smaller during a terminal infection, but from the original report* I cannot see anything peculiar, especially as the patient was taking arsenic and quinine at the same time.

* Liffran, J. Contribution a l'étude de la leucocythémie algue, Thèse, Bordeaux, 1898, p. 66.

Changes in the Red Blood Corpuscles.

Changes in the red cells have not been studied as carefully, perhaps, as they deserve in complicated leukæmias. Out of 18 cases in which the reports are full there was a rise in the number of red cells, simultaneous with the fall of leukocytes, in 8. The difference was often slight, but in 6 it was 500,000 or more (once 1,300,000) per cmm. (Lichtheim). In the other cases the rise was insignificant, or there was a fall. The latter was 500,000 or more in 4 cases; in 1 1,200,000 (Juenger). The great variations in the red count in leukæmia without complications should be borne in mind. A difference of a million or more may be observed in a short time independent of visible causes. The frequency of the rise in the red cells, while the leukocytes and other symptoms seem to indicate the opposite process, suggests a change in the blood fluid as the cause. The fact that 4 cases with marked rise occurred in tuberculosis (Lichtheim, Schmidt, Sturmdorf, de Roth) is interesting, but the cases do not offer a satisfactory explanation. Quincke noticed the unusual bloodlessness for leukæmia, post-mortem, in 1 of his cases. In my second case of tuberculosis the vessels were unusually full of blood.

The histological changes in the red corpuscles are interesting, but variable. Nucleated red cells are not always absent, as some have thought. In Richter's case they appeared during the complication. De Roth noticed many, including some in mitosis. In Juenger's case they were pretty numerous, but disappeared two days before death. In my case these cells were less numerous than before the complication, and increased as the leukocyte count regained a high point, but there were many, even at the lowest period, and often in mitosis. The condition of the red corpuscles should be carefully observed in future.

Qualitative Changes in the Blood, Especially in the Leukocytes.

The earlier observers were unable to notice the finer details in the cells, on account of the lack of methods. Mueller mentioned, in reporting his first case, that mitotic cells (myelocytes) disappeared almost entirely, and the leukocytes changed, so that the leukæmia seemed better, judging from the blood. Mueller's second case, with increase of the leukocytes, has often been misquoted. He himself admitted that no accurate examination of the blood cells had been made. He thought there might have been an increase of polynuclears, as occurs in sepsis, but he also thought the new cells might have been derived from the shrinkage of the enlarged glands, in which case they would hardly have been polynuclear.

Kovacs noticed in his case of influenza with slight decrease of leukocytes that the myelocytes disappeared almost completely, the eosinophiles also, the mitotic cells and nucleated reds completely.

There was an increase of polynuclear cells, so that the blood picture was that of leukocytosis. With the rise of leukocytes the marrow elements reappeared.

Fraenkel noticed no increase of polynuclear cells in his first case, in which, however, the examination was not thorough. In his second case all varieties were reduced.

Richter observed disappearance of mononuclear cells during the complication, with increase of polynuclears up to 90 per cent., the latter in the secondary rise with abscess. Before the complication the two classes had been about equal.

Thorsch, whose case appears to have been chronic lymphocythæmia, with mononuclear cells about 97 per cent., and no eosinophiles or nucleated reds, says that the changes were: mononuclears, 138,600; polynuclears, 1400 at one extreme and 40,585 to 4915 at the other, showing an absolute increase of polynuclears. But this was by no means such an increase as would cause distinct leukocytosis in a non-leukæmic subject, and before the complication, with 113,000 leukocytes at one time, there were 4520 polynuclears. Thorsch suggested that relative increase of polynuclear cells is observed by all in complicated leukæmia, and he made H. F. Mueller's case one of the number, but, as I have shown above, without sufficient basis. Hirschlaff* has a reported case showing that the polynuclears can increase markedly in leukæmia without infection.

In Lichtheim's case of tuberculosis with a fall of 250,000 to 8900, there was a relative increase of polynuclears, viz., from 50 per cent. to 90 per cent., which would amount to a slight increase above normal, but far below the polynuclear count at the height of the leukæmia.

In Baldwin and Wilder's case, without marked alteration of the blood count, there was no notable change in the leukocyte formula.

In Koermoeczi's case of sepsis, with a fall of from 100,000 to 7300, the eosinophiles, myelocytes, and mast-cells disappeared. The polynuclear neutrophiles numbered 75 per cent. (possibly 70 per cent.; there is an error in the report). Just before death counts of 3000 and 2000 were made, with slight increase of the lymphocytes, but no other change.

Adler[32a] examined the blood from Kraus' case, with special reference to the leukocyte formula. Kraus had reported disappearance of the myelæmic condition and the appearance of degenerated leukocytes. Adler shows in tabular form the fall and ultimate almost complete disappearance of the mononuclear neutrophiles (25.50 per cent., 100,514 cells to 0.40 per cent. and 18 cells), the complete disappearance of the basophiles and mononuclear and polynuclear eosinophiles. In the rise before the final fall there was an increase of lymphocytes and decrease of eosinophiles. The eosinophiles disappeared completely with the beginning of severe septic phe-

* Deutsche med. Wochenschrift, 1898, Vereins-Beilage, p. 162.

nomena, and the lymphocytes (small) increased to 40.80 per cent.; large lymphocytes, 1.80 per cent.; mononuclear neutrophiles, 0.40 per cent.; polynuclear, 58.80 per cent., the latter being only slightly increased relatively.

Bezançon and Weil noticed in their case of tuberculosis that the leukocytosis was polynuclear during the infection, instead of mononuclear; basophiles, mononuclears, and eosinophiles were few. There were no nucleated red cells, whereas before there were many, some of them in mitosis. Later, as the infection advanced, the leukocytes rose again (from 19,871 to 45,500), and myelogenous cells, with nucleated reds, increased. In the case of Petit and Weil there was no notable change in the formula. In the case of Weil the polynuclear cells were relatively as well as absolutely diminished; the eosinophiles also.

In Elsner and Groat's case there was an increase of polynuclears and lymphocytes, relatively, and a diminution of myelocytes, as the tuberculosis advanced. But not only in the number of leukocytes, at the lowest 121,000 cells, but also in the formula, the leukæmic character was preserved: polynuclears, 68; myelocytes, 17.5; lymphocytes, 6.5; eosinophiles, 5.2; many normoblasts and megaloblasts.

Sturmdorf observed in his case, in which the number of leukocytes was not much altered during the observations, that each rise in temperature was accompanied by an increase of polynuclears and decrease of myelocytes, "suggesting an intercurrent leukocytosis."

In Wende's case, with a drop of from 45,000 to 600 leukocytes, there was an increase of polynuclears of from 3.4 per cent. to 10 per cent., and a decrease of lymphocytes from 95 per cent. to 88 per cent. in nine days. There are some discrepancies in the author's figures, but they do not materially affect the statements.

In the case of Hirschfeld and Tobias, with a fall only to 110,937 (from 424,000), the polynuclear cells were not relatively increased; the myelocytes were lower then than when the count was above 400,000, but higher (11.5 per cent.) than when it was 300,000 (7.6 per cent.), and there were other variations, but as the author shows, by the counts of another leukæmic patient, the variations were no greater in the case of infection than are sometimes observed without it.

In Murrell's case there was a marked fall in the number of myelocytes, though the differential counts are unusual and cannot be readily compared with others. For example, the eosinophiles are given as 20 per cent. with counts of 20,000 and 29,000; none with 16,200; besides which it is said the myelocytes, 20 per cent., 44 per cent., and 7 per cent. on different days, were chiefly eosinophile.

Parker states that in the low count, 130,000, the polynuclears were relatively fewer than at the height of the leukocytosis, 70.8 per cent. and 57 per cent.; the myelocytes high, 25 as compared with 14; the other forms not notably altered.

Hart found no noteworthy changes in the blood in his case of lymphocythæmia.

Grawitz noticed no change in the formula, either in the fall in the beginning or the rise after the pneumonia or after a turpentine abscess with temporary low count.

In my own case the polynuclears were relatively and absolutely about the same as in normal blood. The lymphocytes were relatively and absolutely about normal, relatively higher than in the high stage, but absolutely slightly lower. The polynuclear eosinophiles were relatively and absolutely low, the mononuclear eosinophiles relatively lower than before, but still considerable, and even higher relatively than at later periods with excessive leukocytosis. The (Ehrlich's) myelocytes were relatively and absolutely low, but even at the lowest count, 9.6 per cent., higher than is usually found in any accidental myelocythæmia. Mast-cells were relatively as in other stages. Degenerated leukocytes were relatively about as high as in the first observation, but higher than they became later as the count rose. Nucleated red cells were relatively much higher than before, reaching 1 to 2.4 at one time, or absolutely 2090 per c.mm. One-fourth were megaloblasts, and a few of these were in mitosis. Nucleated reds were absolutely more numerous at the first count, 1 to 40, or 9074 per c.mm., with a few in mitosis. A few myelocytes also were in mitosis. The reds showed poikilocytosis, vacuoles, and variations in size, as well as polychromatophilia, but without notable changes from the earlier count. No Charcot crystals formed in blood kept for several weeks, and not until the leukocytes had risen to 35,000.

During the rise of leukocytes that began between two and four weeks after the fall was discovered the formula was altered by the relative decrease of lymphocytes, the relative increase of myelocytes, and a slight relative increase of eosinophiles of both kinds. The nucleated reds increased slowly. The large number of these cells during the low leukocyte stage is exceptional. It is possible that they were fewer or absent in the preceding two weeks immediately after the infection, and that they began to reappear in the stage of reaction, but the counts do not support this view.

It appears, then, that the changes in the leukocyte formula are not uniform, though there is a disposition for the leukæmic character to disappear more or less completely under the influence of infections and for the polynuclears to increase absolutely as well as relatively.

When Does the Change Occur?

When the change occurs is a question that cannot be answered very fully, on account of the small number of cases in which the process could be observed from the beginning.

In Eisenlohr's case the glands and spleen diminished daily from

the beginning of the infection and the blood changed simultaneously. As the glands and spleen enlarged again, the blood resumed its former leukæmic character. The decrease lasted fourteen days. One month after the decrease the blood showed proportions of 1 to 4.

In Kovacs' case the blood resembled that of leukocytosis nine days after the beginning of the infection. In twelve days the spleen was smaller and softer. On the tenth day there were few myelocytes; no nucleated reds. Three days later there was an increase, with many myelocytes, and in three more there were 33,000 leukocytes.

In Fraenkel's first case the whole process took place in twelve days. In his second one the leukocytes had fallen to 47,000 by the seventh day, 3800 by the eighth day, 1200 by the tenth day.

In Richter's case the leukocytes fell from 56,000 to 29,000 in two days, but two days later they were 148,000, and six more 52,000.

In Thorsch's case the lowest point was reached in four days. Death occurred three days later.

In Lichtheim's case there was a slow and steady decrease for two months, when death occurred.

In Koermoeczi's case, eight days after a count of 100,000, the leukocytes had fallen to 7300. The patient lived five days longer, with almost the same blood picture.

In Kraus' case the leukocytes fell quickly after infection, viz., from 120,000 to 4600 in one week. In five days more the leukocytes had increased to 9000, and in four more the patient died.

In Weil's case the fall from 270,000 to 75,682 took place in six days; in seven more the number was 66,230.

Elsner and Groat noted a gradual fall of 200,000 leukocytes in three months.

In Wende's case, sepsis in acute lymphocythæmia, the leukocytes fell in nine days from 45,000 to 1600. In Cabot's case the fall to subnormal took only sixteen days; in E. Mueller's case five days.

In Murrell's case there was a fall in three days of from 150,000 to 20,000. Then an increase six months later, and another fall from 167,000 to 16,200 within five weeks.

In my own case of influenza the fall of from 367,070 to 7500 probably occurred within two weeks, but there was no actual observation in that time.

In general, the fall occurs soon after the infection, more promptly in acute than in chronic infections. The cases of chronic infections, however, are too few and too diverse in character to enable us to draw sweeping conclusions. There are also too few cases observed from the beginning to ascertain the first effects of the infection (or intoxication). Perhaps these differ in various cases.

As regards changes in the formula, Hirschfeld and Tobias give a table showing that variations can be observed in the leukocyte formula quite apart from complications, especially notable in the polynuclear and myelocyte count. This will be confirmed by all

who have followed up cases of leukæmia for some time, while changes in the gross number of cells, both red and white, are equally common, and often quite as much or even more marked than in some of the cases examined above.

A very interesting fact brought out in some of the cases, and one that I observed with particular care in my own, is the rapid rise of the leukocytes after a fall to normal, and with a great decrease in the size of the previously enlarged organs. Actual observation must, of course, be the final test of such a matter, but it is easy to understand how a chronic leukæmia may have a sudden increase of circulating leukocytes, including cells not found normally in peripheral blood, or how a so-called pseudoleukæmia may become leukæmic within a short time. These observations do not throw any light on the process by which the new cells get into the peripheral vessels, but they prove that a long time is by no means necessary for a great excess of leukocytes to appear in the peripheral capillaries.

The Effects of Various Processes Other than Infection on Leukæmia.

Finding such striking effects on the leukocytes from the influence of infectious disease, one naturally asks whether other diseases or intoxications may not have similar consequences.

Oette[44] studied the effect of fevers on the course of leukæmia, at the instigation of Mosler, as long ago as 1879, but he was limited by the greater obscurity then surrounding both fever and leukæmia, and did not materially advance the subject.

Freudenstein[31] re-examined it in 1895. He gathered many interesting facts regarding the fever of leukæmia from the early literature, besides the histories of ten of the earliest cases of infection studied here. He concluded that fever is a frequent (63 per cent.) but not constant symptom of leukæmia, and ascribed this to substances derived from broken-down leukocytes, but did not study the possible results of such processes on the leukæmia itself, doubtless because of the difficulties surrounding such an investigation.

Marischler[52] reported a case of lymphatic leukæmia complicated by a Grawitz tumor of the right kidney. There was repeated hæmaturia, considered at first as a result of the leukæmia, but later more properly ascribed to the renal tumor. The leukocytes fell from 96,000 October 16th, 84,000 November 25th, to 48,000 on February 27th, and then rose to 72,000 on the last day. The polynuclears rose from 15.60 per cent. (or 21.70 per cent. at the beginning of the hæmaturia) to 57.60 per cent. The mononuclears fell from 82.30 per cent. (or 76.20 per cent.) to 40 per cent. The difference was still more marked in the blood of the last day. The changes were, therefore, qualitative rather than quantitative. Marischler explained the changes as due less to the hemorrhage than to the carcinoma toxin, a view I do not think free from error. Marischler

gives theoretic reasons, based on experiments, for his view, but the passage of a necrotic bit of tissue, 1.5 cm. by 0.25 cm., shows that the explanation by changes following loss of blood is very near. The author gives the literature of new-growths complicating leukæmia, the only genuine cases he could find being those of Whipham and Lannois and Regaud. In these no effect of the cancer upon the leukæmia was noted.

The literature of leukæmia contains references to cases in which reduction of leukocytes had taken place under the most diverse drugs, such as iron, arsenic and its salts, phosphorus, quinine, oxygen, etc.; but it is suggestive that the drugs that some have found most valuable have failed entirely in the hands of others, without perceptible reasons in the cases themselves. Most of the reports give such scanty details of the blood in the stage of recovery that they cannot be utilized at present. The literature is largely available in the study of Vehsemeyer.[53]

The first to report a careful study of the process were Toulmin and Thayer,[54] who noticed a fall of from 714,000 to 7500 leukocytes in twenty-three days in a patient taking arsenic. Two weeks later there were 9500 leukocytes. The leukocyte formula changed from:

Lymphocytes	0.96	to	6.9
Polynuclear	70.0	to	83.2
Transition	3.0	to	2.5
Eosinophiles	2.3	to	3.0
Myelocytes	23.5	to	4.0

showing a relative increase of lymphocytes and polynuclears. The myelocytes, though much reduced, were still notably high, 4 per cent.

Bramwell[55] mentions a case in which the leukocytes fell from 210,000 to 1600 in thirty-eight days under treatment with arsenic, CO_2, and oxygen, and remained below normal for a month. There was fever and an eruption from unknown cause, so that the case, perhaps, should be included among the infections. The formula was altered as follows:

	Sept. 28.	Oct. 9.	Oct. 15.	Oct. 21.	Nov. 4.
Polynuclear	69.0	70	91	75	62
Myelocytes	26.5	25	3	5	7
Lymphocytes	3.5	5	5	20	31
Eosinophiles	1.0	1+	1+	0	0

Cabot[56] and d'Allocco[57] have reported cases in which the leukocytes fell to normal or below, but, at least in the former case, myelocytes were always present, and in a degree that would in itself excite the suspicion of leukæmia, or, in the absence of acute symptoms, suggest some serious disease of the bone-marrow requiring careful observation.

McCrae,[58] however, published a case in which there was not only no leukocytosis, but no sign of medullary disease. A man, aged twenty-eight years, had medullary leukæmia with a blood count in

the spring of 1898 of 2,680,000 red cells, 584,000 leukocytes. He was put on arsenic, and in August there were only 184,000 leukocytes, and the spleen was barely palpable. In September there were 9250 leukocytes. Arsenic was continued, but in November the leukocytes numbered 178,000. In December there were 98,000; in April, after taking 10-drop doses of Fowler's solution, 5000 per c.mm. The myelocytes numbered 20 per cent. to 23 per cent. in the high stage, but were absent in the low one. The polynuclear leukocytes were 86 per cent. with 9250 leukocytes, normal with 5000. Mast-cells were present only once, in the relapse. Nucleated reds were absent after the first fall.

Taylor[59] has reported 3 cases in which the excessive leukocytes disappeared under the influence of arsenic. The improvement lasted for months, and then relapsed in all cases. A second stage of improvement followed in all; in 2 a third. The changes were qualitative at first, and varied both in quality and quantity at different times. In 1 case all qualitative changes disappeared, and a slight lymphocytosis was the only evidence of blood disease. In the other cases myelocytes persisted to the extent of 1 per cent. to 3 per cent., part eosinophilic. Taylor's discussion of this subject can be read with advantage by all who carry out experiments in the treatment of leukæmia. As in the case of infections, the low leukocyte count does not ensure recovery from the disease. This is shown by many reported cases, including the remarkable one of Saundby,[12] in which the white cells dropped from 540,000 to 8000 in eleven days, but death occurred in coma some weeks later.

It must be remembered that many of the patients whose cases are cited in the early part of this study were taking arsenic, sometimes in large doses, yet I think no one will ascribe the changes wholly or even in part to the drug in all cases. I may add that personally I have never seen a fall below 50,000 leukocytes in leukæmia from arsenic, but in only a small proportion of my cases was it possible to push the drug as it should be.

Under other drugs besides arsenic changes have been observed in the blood count in leukæmia. Von Jaksch[60] treated a patient with thyroiodin and cupric arsenate and noted a fall of from 295,000 to 560,000 to 28,000 in thirteen days, the blood at the latter count giving the picture of leukocytosis with few nucleated reds. The liver became smaller, even before the leukocytes fell. For five weeks the leukocytes were not above 100,000, but in six days reached the former high figure and remained there. Thyroiodin was also given during the rise. The formula two days before the lowest count was: polynuclears, 74.04 per cent.; mononuclear neutrophiles, 10.71 per cent.; polynuclear eosinophiles, 0.70 per cent.; mononuclear eosinophiles, 0.35 per cent.; small lymphocytes, 14.55 per cent.; large lymphocytes and transitional, 3.70 per cent. Basophiles were few at all times, and absent in the earlier examinations.

Pollitzer[61] reported a case of acute leukæmia, in which the leukocytes fell from 91,875 to 8500 in the course of seven days, while the patient was taking quinine in gram doses; fever continued; the spleen grew smaller. The patient died twenty-three days later. Post-mortem the picture was that of acute anæmia gravis with lymphoid hypertrophy of the spleen, intestinal tract, bone-marrow and lymph glands. The author attributes the effect to the quinine, but the fever and the fatal termination suggest that it was due to something else, either an intoxication from the products of cellular break-down or an infection.

In another case of Pollitzer quinine was used in 1.5-gram doses with a rise and subsequent fall, leaving the leukocytes higher than before. The author cites a case of Kuehnau and Weiss,[62] in which a patient with Hodgkin's disease was given pilocarpine and developed acute leukæmia. Sabrazès says that in a case of leukæmia with malaria quinine injections had a happy effect, not only on the malaria, but also on the course of the leukæmia.

Richter and Spiro[63] treated a patient with splenolymphatic leukæmia and apical tuberculosis with cinnamic acid. Intravenous injections of very small doses of this caused the leukocytes to increase within three hours from 170,000 to 560,000. There was also a slight increase of red cells. Polynuclear cells increased from 45 per cent. to 86 per cent.; mononuclears fell from 55 per cent. to 14 per cent.; eosinophiles, scanty before, increased, and nucleated red cells appeared, but the increase of leukocytes soon disappeared. In twenty-four hours the original number was reached; four days after the first injection the number was 46,000, and it then gradually rose to the former point. The process was repeated in two more injections. The spleen and lymph glands grew smaller; the general symptoms improved. The author points out that the experiment shows how much more intensely the diseased hæmatopoietic organs react to irritants than do normal ones, and he compared the results of his experiments with those in some of the cases studied in this paper.

A number of observations have been published on the action of organic extracts and bacterial products upon the leukæmic subject.

H. Heuck[64] at an early period gave tuberculin injections in a patient with leukæmia, who had slight signs in one apex, but no bacilli in the sputum, and no reaction to 5 milligrams of tuberculin. Doses of from 10 to 120 mg., in nineteen injections, caused reactions like those in phthisis. From the twelfth injection (60 mg.; the leukocytes were not counted before) there was a fall in the number of leukocytes each time, quickly returning, though not quite to the previous number; so that at the end of the observation the proportion was 1 to 48 instead of 1 to 57. There was general improvement, with diminution in the size of the glands.

Pal[29] also used tuberculin in a leukæmic patient, and noted a slight

decrease of leukocytes after six hours, followed next day by a rise. In three days the number was 154,000 in place of 134,000, and the glands were larger, but the leukocytes fell to 103,000. A week later with 135,000 leukocytes the polynuclear cells were increased, the temperature and subjective symptoms worse.

Beitzke[65 15] used tuberculin in 6 leukæmic patients in Quincke's clinic. The results were very uncertain, the injections not being continued long enough to permit conclusions to be drawn and other treatment being carried out at the same time. Two patients that gave most distinct evidences of improvement were taking arsenic.

Pollitzer[61a] gave tuberculin in a case of medullary leukæmia in doses of 2 to 200 mg., without reduction of leukocytes, but with increase in the size of the spleen and more marked cachexia. In a case of lymphatic leukæmia tuberculin was given for two weeks in doses of 2 to 64 mg., with a gradual but slight rise of leukocytes, without change in the formula.

Nuclein (Horbaczewski's) was also used by Pal in the case mentioned above, with a fall of leukocytes, but with enlargement of the glands. Pal purposely avoided marked reactions in his experiments, in order to prevent severe effects on nutrition. Pollitzer also used nuclein in both cases cited above. In the first 2-gram doses given for five days had no effect. In the other case there was a slow and immaterial fall, followed by a rise.

Jacob[66] used splenic extract in a patient with leukæmia, giving it subcutaneously at intervals of two to four days. The injections were followed by sweating, anxiety, and dyspnœa, symptoms that Jacob had observed in animals treated with organic extracts, and which he attributed to a leukocyte congestion of the lung capillaries. There was a slight rise in the number of leukocytes, after the early injections, followed by a fall to about half the number present before the experiment was begun. As there was an increased excretion of nitrogen in the urine, Jacob also concluded the injections increased the breaking down of leukocytes.

Here may be mentioned Franke's[67] attempt to use an extract of leukæmic glands. A packet of glands from a case of lymphatic leukæmia was rubbed up with physiological salt solution and kept sterile. Injected into rabbits in doses of 5 c.c. to 10 c.c. there were evidences of breaking down of leukocytes. On account of the patient's condition the treatment could not be carried out as intended.

From these few experiments we learn little more than the need of others, and also something of the practical difficulties of such experiments. The blood must be examined at short intervals after the treatment is given, differential counts must be made, and an almost limitless range of work may be found in studies of the cytolytic conditions at various stages. The careful observation of the body and the subjective symptoms and studies of the metabolism, as shown by the urine, are also desired.

There are still other cases on record that illustrate possibilities in leukæmia.

Strattmann[68] reported a remarkable case, in which a patient with enlarged spleen and leukocytes and red corpuscles in equal proportions underwent an exploratory operation on the supposition that the enlargement of the spleen was due to malignant disease. After considerable manipulation of the spleen for diagnostic purposes, and following massage of the organ in order to overcome possible bad effects of the manipulation, the removal was abandoned, and the patient made a good recovery, so that not only was the spleen smaller, but the blood count was 5,300,000 red corpuscles; leukocytes, 1500.

This may be contrasted with Parker's case, referred to in the early part of this paper. In this a patient with old tuberculosis and enlarged spleen, but negative blood count ("the large lymphocytes seemed more numerous"), was explored, with a view to removal of the spleen. Soon after this the blood was markedly leukæmic.

Here we may allude to Senn's[69] interesting case of leukæmia "cured by Roentgen rays." The symptoms of intoxication, such as high temperature, make one wonder whether there was an intoxication from the absorption of broken-down products of spleen and blood, or, perhaps, an accidental infection, and reports of other cases treated by the same method will be awaited with interest. It is to be hoped also that in such reports the blood will be fully described.

A full and satisfactory explanation of the changes observed in leukæmia under the influence of other diseases does not seem possible at present. We are still too much in the dark regarding the cause of leukæmia, the nature of thechanges in the tissues and the mechanism of the blood changes, and we are only beginning to learn something of the effects of infection and intoxication on the blood-forming organs and the circulating blood. The work done by Muir,[70] [71] Dominici,[72] Werigo and Jegunow,[73] Rubinstein,[74] Lengemann,[75] Roger and Josué,[76] Weil,[77] Flexner,[78] Bunting,[79] and others opens up a most promising field, but at present does not go far in explaining the difficulties in this particular subject.

An early and natural explanation was that diseases associated with leukopenia, or without leukocytosis in ordinary cases caused in leukæmia a decrease of leukocytes. This might apply to miliary tuberculosis, or typhoid fever, such as Eisenlohr's case was supposed to be. But further reports not only opposed this view, but even led to the opposite one, viz., that diseases ordinarily causing leukocytosis have an antagonistic effect in leukæmia.

Ortner[80] offered a plausible explanation, viz., consumption of the body, due to infection, but Beitzke pointed out some important objections. It does not account for the altered leukocyte formula often observed; the change sometimes comes on early, before the exhaustion of the body is evident; at other times leukæmia shows

advanced wasting and cachexia without notable change in the leukocytes. H. F. Mueller's theory is attractive chiefly because of its obscurity. He suggested an "alterative" action, but in the present state of our knowledge this does not explain anything. The leukocytolytic theory of Fraenkel is also attractive. It seems borne out by the author's observations on degenerated leukocytes in his own cases, and the increased excretion of uric acid. It seems analogous to the rapid disappearance of certain tumors, some of which (sarcomata) closely resemble leukæmic growths, under the actions of poisons like arsenic, or those of certain infections, as erysipelas. Recently the chemotactic theory has become more prominent, and has received the support of Ehrlich, whose influence in the study of leukæmia is deservedly so great. Quincke's objection, that no evidences of transfer of leukocytes are present, might be explained by a rapid breaking down of the cells.

It seems to me the process in most cases is complex. Breakdown and consumption must occur in cases with severe cytolytic poisons, and in some must preponderate. In others chemotactic processes will be most important, and innumerable variations in the clinical course and the blood picture will probablydepend partly on the kind, extent, and intensity of the intoxication, partly on the histological peculiarities of the new-growths, and the capacity of their cells to enter or be poured into the circulation. Thus, in acute lymphatic leukæmia, the changes will not be the same as in the chronic myeloid alteration of all the blood-forming organs.

Finally, the question as to therapeutic bearings must be met. It is easy to understand how many have looked upon the changes observed in cases cited above as evidences of healing. The most striking sign of leukæmia, the excess of leukocytes, disappears, and sometimes the spleen and lymph glands return to their normal size. Yet that the change is not wholly favorable appears from the fact that no case has really recovered. Most patients died while still under the influence of the process that was thought to have healed them, and, although some seem to have had their lives prolonged, none have lived longer than many leukæmics without such complications.

Weil has suggested that the action of the complicating infections is too "brutal," and this may be so, although the cases hitherto observed show considerable variation in severity. But, considering the hopelessness of the ordinary treatment of leukæmia, it seems that carefully planned experiments, either with bacterial products or organ extracts, might show a more safe and permanent result. I need not go into the details of such experiments, but may point out the necessity of thoroughness of the observations as an essential. Previous experience with the substances to be used, either on men or animals, is desirable, while a familiarity with the methods of blood examinations is indispensable.

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CARCINOMA OF ABDOMINAL CAVITY; PUNCTURE OF INTESTINE DURING PARACENTESIS ABDOMINIS; PRESENCE OF CARCINOMATOUS FRAGMENTS IN ASCITIC EXUDATE.

REMARKS ON CYTODIAGNOSIS.

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The following case is of interest as showing the difficulty of diagnosis of abdominal disease, the danger of even the most carefully performed paracentesis, and the value of microscopic examinations of exudate, etc.

Mrs. B., aged sixty-eight years, complaining of abdominal distention, dyspnœa, indigestion. Family history unimportant; acute Bright's disease twelve years ago, with apparent complete recovery as far as symptoms showed. Six months previously the patient noticed

abdominal enlargement, which, being naturally corpulent, she attributed to fat, discovering soon, however, that fluid was present. Fluid increased, persistent discomfort after feeding developed, and, later, diarrhœa. The urine was markedly diminished, albumin and casts were present, and the patient became steadily weaker.

Examination revealed only ascites, hidden somewhat by a thick apron of fat; liver dulness present, as far as could be judged, in normal extent; œdema of legs, loud systolic apical heart murmur, slight dulness and few moist crepitations at base of lungs.

Patient had been tapped one month previously, eleven quarts of dark fluid being removed, a considerable amount of fluid blood coming away at finish of operation.

At the second tapping (the first while in our hands) twelve quarts of a bloody fluid were removed; no free blood flowed; liver dulness did not appear quite as extensive as normal; patient seemed much relieved after operation, and gastric symptoms abated.

Ten days later a third tapping brought away six quarts of fluid resembling that of the previous tappings, some gelatinous and granular material coming away just before removing the cannula.

The operation in each case was performed by a surgeon, local cocaine anæsthesia and incision through the skin between the navel and pubes preceding the introduction of the trocar; little if any pain was experienced by the patient; a large apron of fat reaching to the pubes interfered greatly with the drainage of the abdominal cavity.

In six hours after this (third) operation there was a complete collapse; temperature previously, 99° to 100° F., dropping to 97° F.

Tympanites developed quickly; abdominal pain and vomiting, rapid, weak pulse, and rising temperature made us suspect a bowel perforation and subsequent peritonitis. Death took place in three days. At no time after the first appearance of fatal symptoms did the patient's condition seem to justify any further exploration of the abdomen, and, as the examination of the fluid and material removed made the presence of cancer probable, such steps were deemed inadvisable in any case.

The clinical picture in this case was from the first obscure; the huge accumulation of fat present in the abdominal walls precluded any satisfactory examination; at times, even before twelve quarts of fluid were removed, fluctuation was indistinct; there was no anæmia, the withdrawal of so much fluid into the peritoneal cavity causing, in fact, a distinctly concentrated condition of the blood, as is sometimes seen; cirrhosis of the liver or carcinoma of some abdominal or pelvic organ were considered the most probable causes of the recurring ascites and associated symptoms.

The bloody appearance of the first fluid removed was suspicious of malignant or tubercular disease; neither suspicious cellular elements nor bacilli were to be detected. The second fluid removed

was, on the contrary, suggestive from the outset. The colloid-looking lumps in the precipitate passing ready formed through the cannula must necessarily have been fragments of some tumor formation or material direct from the intestine; as a matter of fact, both substances were present. Further examination showed specific gravity, 1020; albumin, about 0.3 per cent.; sugar, 0. Microscopically fibrin, intestinal material, starch, vegetable fibres, meat fibres, and some bunches of leptothrix (proving that the bowel had been punctured) were readily seen.

The puncturing of the intestine in paracentesis abdominis, although always considered a real danger, must be considered as infrequent; in this case more than usual care had been taken; it is possible, of course, that portions of the intestines had become adherent in some part and presented resistance to the trocar.

The cellular elements in the exudate attracted our attention from the outset; quite numerous red blood cells were, of course, to be seen; distinct pus cells were few; on the other hand, epithelioid cells or cells resembling the larger lymphocytes were numerous, either single or grouped as in the drawing (4), showing fibrillar intercellular structure, and columnar cells in groups (3), evidently parts of distinct glandular structures, were in evidence. The arrangement and variety of these first-mentioned cells cannot be said to be diagnostic of carcinomatous conditions; similar-looking cells are present in tubercular exudates; their presence in masses, as in the figure, was suggestive and suspicious, more from its gross appearance than from the character of the individual cells; the distinctly glandular-looking cells, arranged in columns (3), could only be intestinal or from adenocarcinomatous new-growth.

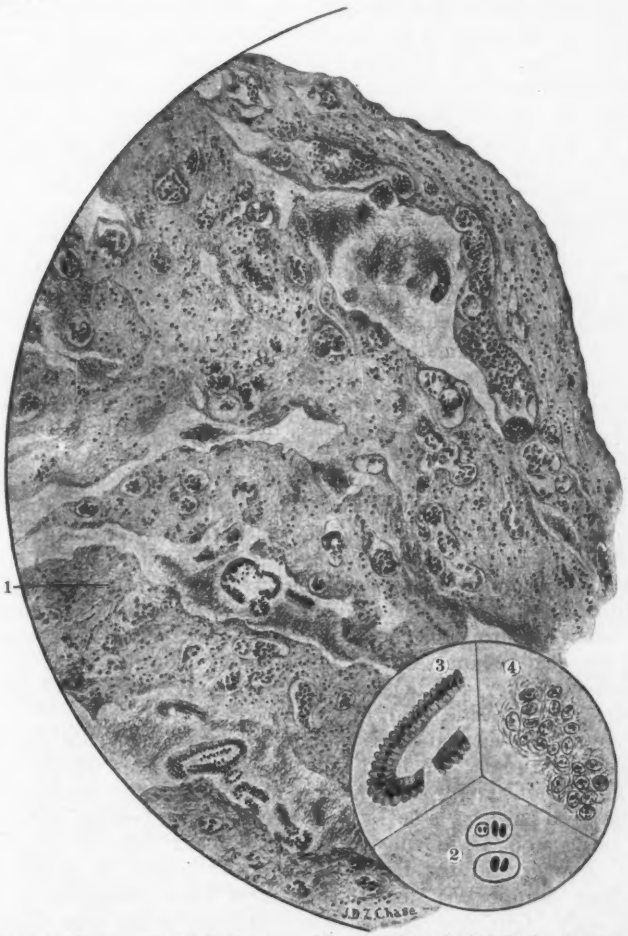
The colloid masses referred to, on being teased out, gave the picture as shown in the figure and just described; it seemed certain thereafter that the cells of the exudate were the colloid elements. Hardened and prepared the colloid masses gave the picture shown in the drawing (1), which can be briefly described as "adenocarcinoma showing advanced colloid degeneration," probably from the suggestive follicular structures connected with the intestine.

The diagnosis of malignant disease in various parts of the body, by means of the character of the cells found in the exudate, has been for some time a rather fruitful field of speculation. We are at present, however, much nearer an accurate working knowledge on the subject, thanks to the careful work of Dock and others; but the readiness with which the earlier writers in the earlier microscopic days accepted various atypical cellular modifications as evidence of malignant disease is striking.

Quincke considered cells of large size in any number, either separate or grouped, as most suggestive; the presence of the glycogen reaction was considered to make the diagnosis almost certain.

Eichhorst makes the statement that "especially in cancer of the

pleura we find in the exudate not rarely abundant fatty granular cells and cells with multiple nuclei," which are characteristic of cancer. Geigel and Voit were practically in accord with this view in 1895.



1. Fragment of tumor removed during paracentesis. 2. Cells and cell inclusion from a case of carcinoma recti. 3 and 4. Types of cells and arrangement found in fresh exudate.

Rieder, in the same year, in a detailed and well-illustrated article, is distinctly of the opinion that polymorphonuclear endothelial cells, cells showing atypical mitoses, vacuoles, and having a tendency to appear in clumps, are certainly malignant. Neelsen agrees with this view.

The description and illustrations of the cellular findings in malignant and other exudate, as given by Dock several years later, show clearly that these views must be taken cautiously, since all the cellular changes described by the observers as characteristic of malignant exudates were found by him in conditions distinctly not malignant, although, as he admits, in much smaller numbers.

Dock agrees with Rieder as to the possibility of distinguishing cancerous from tuberculous exudates from a consideration of the cellular constituents thereof. In the latter, as a general rule, according to both observers, the great variety of cells, the mitotic and amitotic figures are rare; a small cell, with the general characteristic of a lymphocyte, being more usually seen.

Warthin a few months later reports the ready diagnosis of a primary sarcoma of the pleura from the large number of spindle cells found in the exudate; these spindle cells differed rather materially from the ordinary fibroblast found in pleural exudate in not showing branching processes and in their regularly more oval-shaped nucleus; numerous symmetrical mitoses were also present. A comparison of these cells with those present in serous and fibrinous pleural and pericardial exudates and with normal pleural cells does show, in the gross, some difference, but certain characteristics are possessed by all. The great number of the spindle cells is probably the most suspicious character of the exudate in his case.

Hemmeter insists upon the regularity with which cells showing mitotic figures, symmetrical and asymmetrical, may be found in the washings from cases of carcinoma of the stomach.

A more complete microscopic picture and a certain diagnostic feature is presented in cases in which (as in ours) tumor fragments are removed during the simple operation of paracentesis or lavage. The reported instances of this happening are not numerous.

Steiner, Rieder, and Lenhartz give instances of recovery of tumor particles from ascitic fluid.

Prentess, Girvin and Steele found particles of malignant growths in pleural exudate; the fixed and stained specimens usually have shown very distinctly the nature of the new-growth; examination of the fresh particles is not always so certain, the cellular structure not being so clear. Ordinary small endothelial cells or lymphoid cells entangled in the fibrin coagulum of simple or tubercular exudates can present suspicious features when examined in the fresh state. Our own experience in cytodiagnosis has been of more or less interesting nature. In our cases of simple or supposed tubercular pleurisies it has been easy to demonstrate the preponderance of the lymphocyte-like cells described now as the most common cell in these conditions. The large endothelial cells, at times mononuclear, at times polynuclear, were regularly seen in small numbers.

In several fluids from spinal punctures, in which no pneumococci or other micro-organism could be demonstrated by stain or culture,

but which were also negative for tubercle bacilli by inoculation, the same lymphocyte-like cell was the prevailing element.

No exudates due to the more common organisms, streptococcus, pneumococcus, or typhoid bacillus, have come under our observation since this paper was begun. It is now generally found that in such exudates the pus cell, the ordinary polymorphonuclear cell, is in excess.

In a gelatinous, chocolate-colored sputum from a patient with persistent cough and wasting, we were struck by the almost purely cellular condition of the material. Closer examination showed a total absence of the ordinary polymorphonuclear leukocyte, and the presence of such dense numbers of mononucleated round or oval lymphoid-like cells as to give the idea that one might be observing an extremely cellular tissue, such as sarcoma, rather than an exudate or secretion. These cells stained readily when fresh, were non-granular, the size of a medium-sized or large lymphocyte; no mitoses or multinucleated elements were made out; nucleated stains showed a reticulated, well-formed nucleus. The findings of the subsequent autopsy were given to be a "tumor of the lung." A further application of the cytodiagnosis was shown in the case of a patient suffering from an intermittent diarrhœa, associated with bloody, mucus-like discharge. Numerous mononucleated and multinucleated cells of epithelioid character were demonstrable, and were in themselves suggestive of a condition other than a simple inflammatory one, but the most suspicious elements were cells such as pictured in the drawing (2), with their cell inclusions. The association of these bodies with carcinoma and their supposed parasitic nature is now a matter of every-day discussion, and needs no comment.

I do not know of their being described previous to this in exudates, etc. Proctoscopic examination and subsequent history revealed malignant ulceration of the upper rectum.

We were singularly unfortunate in our cases in not being able to demonstrate mitotic figures, and hence the question of the diagnostic value of these figures in the cells of exudates cannot come into consideration. Steiner failed to find mitoses in his case. The condition of the new-growth, whether rapidly growing or not; various physical states, such as serous membrane irritation, probably account for the presence of these figures. I must agree with recent observers "that the presence in exudates of *many* cells showing mitosis will, in most cases, allow us to make a diagnosis of malignant disease;" such cells are certainly rarely present in other conditions, and then but in scant numbers. Small cells grouped in masses, as shown in the drawing (4), are suspicious, and were enough in our case to convince us of the malignant nature of the trouble. One does not often find such groups in simple conditions, nor could one readily explain their presence in such; masses of desquamated endothelial cells do not show the intercellular fibrous strands as in the figure; moreover, the large size of the endothelial cells would

show their nature. Large, multinucleated, endothelial-like cells are more common in malignant disease, but are seen frequently in other conditions.

Cells of such glandular type and arrangement as found in our case, and pictured in the drawing (3), could not be passed over. In this instance not only the nature of the new-growth, but its situation or the situation of metastatic accidents is demonstrated.

One of our recent cases is of interest, and, at the same time, shows the limitations of cytodiagnosis. In this instance, a few days after an operation removing the right breast for what has been shown to be a cancerous degeneration of an adenofibromatous tumor, a pleural effusion, with fever, developed. Repeated aspirations (3) were necessary to relieve the patient. Subsequent metastasis, developing rapidly along the incision, led us to consider the condition as probably due to extension of the disease to the pleura. The fluid of the various tappings showed at no time, however, any cells suggestive of cancerous vegetation. On the other hand, the preponderance of 98 per cent. to 99 per cent. of small mononuclear leukocytes was always evident. There has been no reaccumulation of fluid since the last aspiration eight weeks ago, the fever falling to normal after the first and remaining there. The cellular condition in this instance is suggestive of a tubercular more than a malignant or mechanical pleurisy.

One must certainly admit that considerable information and help may be derived from careful examination of exudates, etc., as to their cellular constituents. The presence of cells in any number should lead to more careful consideration of their type, arrangement, and nuclear condition.

In a majority of instances one may suspect malignant disease if large numbers of nuclear figures, typical or atypical, are present; their absence, on the other hand, by no means, excludes the possibility of malignancy. Occasional nuclear figures are to be found in other conditions.

Endothelial cells with many nuclei are probably but not certainly more numerous in cancerous exudates. Cells of exudate tending to appear in bunches or groups with intercellular fibrillæ (as shown in 4) are, to a degree, suspicious; apart from fragments of squamous epithelium and desquamated flakes of large endothelial cells, there are few conditions which would cause cells not of these varieties to appear in compact masses. Small groups of lymphocytes or pus cells, of course, are often seen.

Unusual cells of glandular or other type, or such as are depicted containing cell inclusions, must be given a significance of their own. The question of cytodiagnosis of tubercular and other exudates has been of late freely discussed, and it seems probable that tubercular exudates are more or less regularly associated with lymphocyte-like cells, particularly after the first few days.

Mechanical exudates show more often numbers of large endothelial cells, often in large plaques, the "placards" which Widal and Ravant consider pathognomonic of mechanical exudates or transudates.

Infectious pleurisies, etc., are found to have the polymorphonuclear leukocyte as the characteristic cell of their exudate.

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THE CLINICAL BEHAVIOR OF THE LYMPH GLANDS IN TYPHOID FEVER.

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So far as I can determine by examining the most important recent works on typhoid fever and by searching through any papers with suggestive titles, the statement that widespread enlargement of the lymph glands, recognizable clinically, occurs in typhoid fever has not been made. It is known that the lymphatic enlargement found at necropsy is not limited to the tissues in the intestine and to the glands in the direct path of the lymph stream from the intestine. Post-mortem findings of enlargement of the inguinal and the peri-œsophageal glands are sometimes noted; and lymphatic tissues that are even as distant from the intestines as are the tonsils occasionally show enlargement, and in some instances are probably directly involved in the typhoidal process. Indeed, typhoid fever plays its part so largely in lymphatic tissues that it is to be expected that it should, at times, produce widespread glandular enlargement, readily recognizable at post-mortem, particularly since the disease is well known to be a general bacterial infection and not a local process.

Clinically, however, in cases in which it is necessary to distinguish between typhoid fever and other diseases in which glandular enlargement is common, the discovery of many readily palpable glands is usually accepted as being a point in favor of the last-mentioned class of diseases and against typhoid fever.

In May, 1903, in the course of my services at the Episcopal Hospital and at St. Christopher's Hospital for Children, I encountered within two weeks 3 cases of rather peculiar nature, in which glandular enlargement was a point of some importance in the diagnosis. The first case was in a boy aged six years. In the course of typhoid fever, and while rötheln was prevalent, this child developed a rötheln-like rash and was found to have easily palpable glands in the occipital and the anterior and posterior cervical regions, as well as in the axilla and the groin; and subsequent observation showed that these glands exhibited a slight further increase in size and a distinct increase in number. The absence of any other new symptoms, the fact that the fever was dropping at the time and continued to decrease, the lack of any influence upon the patient's general condition, and the rapid disappearance of the eruption, without any trace of desquamation, led me to decide that this was merely an accidental rash.

In the second case, that of a boy, aged eighteen years, the presence of swollen and slightly ulcerated gums, with some excess of leukocytes, and with an absence of any distinctive evidence of typhoid fever, suggested the possibility of an early acute leukæmia. This patient showed a small number of readily palpable anterior and posterior cervical, axillary, and inguinal glands; and within a few days the palpable glands were found to be increasing in number, though not distinctly increasing in size. He soon developed spots and a Widal reaction, however; the leukocytosis disappeared, and he rapidly settled into a course of typical typhoid fever, no complication, except the mild grade of stomatitis, being discovered.

The nature of the third case still remains somewhat obscure, although I believe it was typhoid fever. In considering the possibility of syphilitic fever in this case, I found easily palpable anterior and posterior cervical, axillary, epitrochlear, and inguinal glands. The man denied the possibility of syphilis, however, and showed no primary lesion, and he had no subsequent manifestations of that disease. While he had no absolutely characteristic evidences of typhoid fever, that diagnosis remains the most probable.

These observations led me to make notes at various periods of the disease in a series of cases of typhoid fever. As a result, I think I may state without hesitation that in a considerable number of cases widespread glandular enlargement that is, to be sure, slight, but sufficiently marked to be discoverable clinically, occurs in this disease; and in some instances the glandular enlargement is as marked as that which usually occurs in certain other infectious diseases, and is usually looked upon as somewhat distinctive of those diseases.

The regions that I especially observed were the groin, the axilla, and the anterior and posterior portions of the neck. In some cases the condition of the epitrochlear and the brachial glands was also noted. In most cases the enlargement observed was very slight; it was some-

times so slight that I doubted whether it could be considered to be actual enlargement. The most common condition was the appearance of many glands about the size of buckshot or a little larger; these were, as a rule, especially easy to palpate in the axilla and the groin. Little attention was paid to such a condition of itself, as I appreciated the fact that glands of this size might readily have been present from the beginning and have become apparent only because of emaciation. Very frequently, however, I noted, during the course of the disease, the development in the axilla and the groin of glands that I have described in the notes as varying in size from that of small peas to that of hazelnuts, while in the neck they were often noted as being of the dimensions of small peas. In some of these instances such glands were present in small numbers on admission, but I noted a distinct increase in their number during the course of the disease. As a rule, the occurrence of glandular enlargement could be determined only by painstaking and deliberate examination; occasionally, however, it was sufficiently marked, especially in the axilla and in the neck, to be apparent upon rather hasty palpation. In the groin the conditions were not quite so patent, because most of these patients, as is so very common, showed here some old enlarged glands in the beginning; hence a little more care was necessary in this region, in order to determine whether these glands were enlarging and whether new ones were appearing.

I am, for several reasons, disposed to be very guarded in using my figures as to the frequency with which enlargement can be noted. In the first place, the number of cases that I have observed is too small to be distinctive. In the second place, the circumstances attending the observation of such cases are likely to lead one astray; that is, typhoid fever patients usually emaciate rapidly during the course of the disease, and then rapidly put on flesh after convalescence has begun. In consequence of this, glands already palpable would become more distinctly so; and others, not at first palpable, would appear as the result of the emaciation; while, when fat is being reacquired, the conditions are reversed. This tends to give one the impression that the glands are showing slight enlargement during the course of the disease, and that this enlargement is disappearing during convalescence. Furthermore, anyone that makes a practice of searching for small lymph glands will agree with me that in the most varied conditions a few may often be found high up in the axilla, while they are somewhat less easily and less frequently discovered in the anterior and posterior cervical regions, though common here. Naturally, also, the more frequently the search is repeated, the more often will glands be discovered and the greater will be the number found; hence, repeated search at various periods of the disease might give one the impression that the glands are increasing somewhat in number, when this is not the case. I have been careful to exclude, as far as possible, these sources of error,

and have weeded out from the positive group the cases in which I thought that the notes of increase in the size or the number of the glands might have been due to mistakes in observation; but even after having done this, I am inclined to think that my figures show a greater frequency of the condition than is quite correct.

The total number of cases that I observed was about 60. Some of them, however, were seen only late in the course of the disease; and another group exhibited complications like furunculosis. The conditions in the former were not distinctive, and in the latter any glandular enlargement might readily have been due to the secondary infection. I have, therefore, excluded all these cases. This brings the total number down to 43. Of these, 7 at the time my service ended were still in such an early stage of the disease that the behavior of the glands during the course of the disease could not be determined properly, so that the cases in which satisfactory notes have been obtained number only 36.

In these 36 cases I observed the occurrence of glandular enlargement during the course of the disease in 25 instances; in 4 the conditions were doubtful, and in 7 there were no determinable changes in the glands.

At the time of admission, 12 of these 25 had enlargement of the peripheral glands other than the inguinal; they likewise had inguinal enlargement, but, of itself, this is, of course, of little interest. Twelve showed no enlargement of other glands than the inguinal, and in 5 of these cases no inguinal enlargement could be observed. Three of the last-mentioned 5 cases occurred in young boys. In the 1 case remaining of the 25 I have no notes made upon admission.

Notes during the course of the fever show that in 22 of the 25 cases there developed distinct enlargement of the axillary and the cervical glands; in 1 other case glandular enlargement, noted upon admission, distinctly decreased before the fever ended, while in the 2 remaining cases the condition of the glands was doubtful during the course of the fever. Although these 2 cases last mentioned were doubtful at this period, they are included among the positive cases because, in early convalescence, it was determined that there had been a decided increase in the size and number of the glands.

Upon discharge, 16 showed a distinct decrease in the glandular enlargement; in 6 it persisted about as it had been when last noted; in 2 there was, as mentioned, a distinct increase in the size of the glands, and in 1 the axillary glands were noted to be decreased and the cervical increased.

Of the 7 cases mentioned in which the notes covered too brief a period to allow of their inclusion in the above figures, 1 showed distinct decrease in the glandular enlargement within a week after admission (he had been ill twenty days when admitted), in 2 there seemed to be a distinct increase in the size of the cervical glands, and in 4 the notes were absolutely indistinctive.

While I have stated that I am not convinced that enlargement occurred in all the cases in which my notes indicate that it did, I have no question concerning most of the cases that I have included as positive, and there were certain cases in which the changes in the glands were so readily determinable that there could be no possible source of error in the observations. There were, for instance, three boys, aged between twelve and fourteen years, that upon admission showed, after the most careful search, no enlargement of any glands, except for a very few, about the size of buckshot, in the inguinal region. During the course of the disease these patients all developed many palpable glands, a few of the largest becoming the size of small hazelnuts, many reaching the dimensions of moderate-sized peas, and numbers of buckshot-sized ones becoming palpable. In two of these boys the glandular enlargement decreased decidedly during defervescence, even before the patient was being fed more freely, and hence before any flesh was being put on; and in both these patients the enlargement had practically disappeared before their discharge from the hospital. In the third case the enlargement, although it decreased somewhat, persisted until the time of discharge.

There were also several cases of relapse in which changes in the glands could easily be followed. In one of these it was noted that upon admission the inguinals only were enlarged. Within a week the cervical, axillary, and epitrochlear glands had become easily palpable. Two weeks afterward, when the patient's fever had disappeared, the glands were found to have decreased markedly in size and number. Ten days later, after he had been for a week in a relapse, the enlarged glands were found to be much more numerous than they had been in the primary attack; and the number of these glands continued to increase up to the time of his discharge, which was somewhat premature. (Two weeks later, just after I left the service, this man was admitted in a second relapse.)

In another case there were no notes upon admission; but during the course of the disease the inguinal, axillary, and cervical glands were felt in moderate numbers and were the size of peas. At the end of an afebrile period of a week the axillary and the cervical glands had decreased greatly in size; the inguinals remained unchanged. Toward the end of a relapse of two weeks' duration the axillary and the cervical glands were found to be again as large as peas or larger, and to be much more numerous than they had been before. These glands had decreased to the size of buckshot before the patient's diet was increased, and remained in this condition at the time of his discharge.

In a third relapse-case only slight glandular enlargement, if any, could be determined to have occurred during the primary attack, while during the relapse there was distinct and general enlargement.

Notes were not made with sufficient frequency during the course of

these cases to determine definitely when the enlargement occurred. In some instances it seems to have appeared early in the disease, for a number of patients were admitted at the end of the first week with a large number of palpable glands, and this enlargement disappeared late in the course of the disease or during convalescence, indicating that it had been due to the attack of typhoid fever. In most instances, however, the enlargement appeared to develop—most strikingly, at least—in the latter part of the disease; and in a number of cases increased enlargement or the first definite enlargement was noted during early convalescence. As already indicated, it had, in the majority of cases, disappeared to a greater or less extent before the discharge of the patient, but in about one-quarter of them it persisted unchanged up to the time of discharge.

I at first thought that by carefully observing the glands it might be possible to learn some facts that would be of value in diagnosis. It seemed possible, for instance, that this might afford some help in distinguishing between typhoid fever and obscure cases of tropical malaria. There were a number of such cases in the wards during this period, and in 2 of these repeated searches for the plasmodium, even when instituted by a person so skilled as is Dr. Ghriskey, failed to show the parasites; although they were ultimately discovered. The glands in these patients were observed persistently, but showed no enlargement.

It likewise seemed possible that in acute tuberculosis glandular enlargement would occur less commonly and less rapidly and would not be widespread. Two cases of acute pneumonic tuberculosis were observed during this period in the ward; they showed no general glandular enlargement. Perhaps in disseminated tuberculosis and some other conditions the enlargement of the glands might be of interest in the diagnosis. On the whole, however, I believe that it is of little consequence in this way, for the enlargement in typhoid fever tends to occur late, and frequently so late as to be, for this reason if for no other, of no diagnostic importance; and it is also often so slight that it can scarcely be of much help. Furthermore, I do not believe that slight enlargement of the lymph glands, such as I have described as occurring in typhoid fever, can be of great importance in distinguishing this condition from other infectious diseases, for I am convinced that glandular enlargement occurs much more frequently in many infectious diseases than the common descriptions of these diseases would lead one to believe. This has recently been clearly shown by Schamberg to be true of scarlet fever and also of measles; and there is certainly a growing recognition of the fact that glandular enlargement is common in many of the other bacterial infections.

The possible bearing of the glandular enlargement upon prognosis has interested me somewhat, because, as I have already stated, the enlargement was in most cases observed rather late in the disease, a fact suggesting that it might have something to do with the pro-

duction of immunity, instead of being merely an expression of general infection of the lymphatic apparatus with typhoid. The 43 cases that I have referred to all recovered, so that I can make no direct statement as to its possible bearing upon prognosis. During the time that these observations were being made there were three deaths from typhoid fever in the wards; but all these patients died of severe complications that had no direct connection with the severity of the typhoid toxæmia, and all these cases have been excluded from the list—two because they had furunculosis, and the other because I had no notes until toward the end of the patient's life. It is possible that more careful and more extended observation will show that the degree of the glandular enlargement may be made to influence the prognosis. This is, at any rate, suggested by the fact that the enlargement occurs most markedly as convalescence is approaching, as well as by the fact that the most marked enlargement of the glands was observed in several of the mildest cases. Furthermore, the behavior of the glands in several cases of relapse suggests this possibility. As stated, a limited glandular enlargement was observed in a number of cases during the primary attack; while during the relapses, which were followed by definite recovery, a much more marked enlargement occurred. The last-mentioned fact, however, indicates that glandular enlargement, unless quite marked and general, cannot have any important bearing upon prognosis, for readily discoverable enlargement may be followed by relapse.

I thought that the development of decided glandular enlargement, together with the usual signs of approaching convalescence, might afford some indication that the disease is actually about to terminate, and might be helpful in recognizing early the not uncommon cases in which the afebrile state is but slowly established or the disease is much prolonged. It cannot, however, prove of great importance in this way, as is indicated by the conditions just mentioned in connection with relapse; a recognizable and fairly considerable glandular enlargement may certainly occur, and yet be followed by a distinct relapse.

These observations concerning prognosis were suggested by the extensive discussion in recent years concerning the tissues active in the production of immunity. The behavior of the glands in the cases that I report has a certain degree of interest in this connection, although, of course, a limited one. The fact that the glandular enlargement occurred so generally in cases that ended in recovery and that it developed late in the disease, as convalescence was being established, seems to suggest that the lymphatic tissues were active in these cases in establishing immunity, and thus to add some support to the view that the lymphatic tissues play an especially active part in this function.

The chief interest in these observations, however, lies in their relation to diagnosis. Glandular enlargement, unless very marked,

cannot be considered a strong point against typhoid fever, for enlargement of the degree that is, for example, usually seen in syphilis is not very uncommon in typhoid fever, and a somewhat lesser degree is very common.

RENAL DISEASE OF PREGNANCY AND RETINITIS ALBUMINURICA.

WITH REPORT OF A CASE.

By Leo Jacobi, M.D.,
of New York.

Many systemic manifestations of pregnancy are situated on the border line between the physiological and the pathological. Vomiting, œdema, hypertrophy of the heart, nervous disturbances, etc., are all illustrations of a fluctuating equilibrium. Still more important are the renal changes accompanying the condition, and these have, in the course of time, given rise to abundant discussion and discord; naturally enough, for no fixed line of demarcation can be traced between the normal and the pathological. Neither should this nonplus us, if we only recollect the gradual character of all fundamental transition, as between life and death, animal and vegetable, and many another.

It is granted by all that certain changes are found in the kidneys of the pregnant woman; but divergence of opinion begins the moment we ask, Are these changes organic and abiding, or merely functional and transitory? The practical bearing of the answer needs no emphasis, and yet a definite answer is not forthcoming.

Equally deplorable is the obscurity prevailing in respect to that most important result of renal disturbance—albuminuric retinitis—occurring in pregnancy.

The writer does not presume to deal exhaustively with these formidable problems. He wishes merely to report an interesting case and to indulge in a few warrantable inferences.

Mrs. Dora M., aged thirty-three years, a large, strong, and well-built woman; has been married thirteen years. The first conception took place soon after marriage. In the third month of this first pregnancy she sought the aid of a midwife, who performed criminal abortion. Since that time the patient suffered from a chronic inflammatory gynecological affection, for which she underwent repeated courses of treatment at home and abroad. Conception did not occur again for eight years, in spite of varied therapeutic measures directed to that end.

Four years ago she again went abroad, and her husband seized the opportunity for acquiring syphilis. He presented himself with

a chancre and was properly treated from the start. He has remained well, at least to all appearances.

The wife returned soon after his infection, and, in spite of all admonitions, sexual relations were resumed. What seems to be noteworthy, the woman, who had been sterile for eight years, now conceived promptly. Though she never showed any manifestations of infection, the baby was born prematurely (eight months) in a macerated condition.

She now underwent varied but irregular antiluetic treatment with mercury, potassium iodide, and iodipin internally. Conception took place promptly, and one year after the first confinement she was delivered at full term of a macerated fœtus. In view of this renewed evidence of latent disease, she submitted to a course of specific treatment by subcutaneous mercurial injections.

After an interval of some two years she conceived again, the last menstruation having begun October 20, 1902. She enjoyed apparent good health up to April, 1903, when she first complained of severe headaches. She was instructed to send her urine for examination, but, the headaches having left her in the mean time, she neglected to do so.

Four weeks later she presented herself with a train of disturbances: nose-bleed, headache, vomiting, cough, dyspnœa, palpitation, diplopia, blurred vision, and impaired hearing. She passed but little urine and noticed that it foamed on passing (a sign of albuminous liquids noted, I think, by Hippocrates). Examination revealed the presence of considerable albumin. *The excretion of urea was diminished.* With the exception of slightly swollen eyelids, no œdema could at any time be discovered.

An ophthalmoscopic examination was made on June 1st by Dr. Schapringer, of this city, and his report stated the presence of "retinitis albuminurica."

The patient was now kept in bed on a milk diet and treated with hot baths and antiluetic as well as eliminative medication. No improvement followed, the condition becoming gradually but steadily worse. Muscular twitchings in the legs appeared from time to time, and, in addition to the uræmic manifestations (headaches, vomiting, insomnia), *a right-sided facial paralysis supervened.* Under these threatening toxæmic circumstances delay was fraught with danger, and the induction of premature labor was decided upon *ex consilio.* The patient was transferred to a private hospital and interference inaugurated on the morning of June 10th by packing the cervix with iodoform gauze. Slight pains appeared during the day and some bleeding took place—a welcome occurrence, in view of the high vascular tension. Twenty-four hours after the packing the cervix was sufficiently softened to permit rapid dilatation with the fingers under chloroform anæsthesia. The hand was now introduced, version performed, and the baby extracted without difficulty.

The puerperium ran an uneventful course, and on June 25th the patient returned home.

The child, a boy, weighing three pounds and five ounces, showed no signs of syphilis. He was tentatively placed in an incubator, but did not bear the latter well and had to be removed. Surrounded by hot-water bags, he lived two weeks.

Promptly following delivery a striking improvement became evident in the mother's condition. The vomiting, headaches, and a host of uræmic complaints ceased at once. She remained sleepless for two nights, but afterward slept soundly. Her appetite returned. Vision, which had been so dimmed that she could not recognize a person at her bedside, began to clear up noticeably, and by the end of the first week she was able to read large print. She passed an abundance of urine which, three days after delivery, contained only a trace of albumin.

The improvement of vision was henceforth progressive. An ophthalmoscopic examination made on July 20th showed only traces of the former white deposits on the retina. Some astigmatism was also found. With correcting glasses vision soon became perfect.

The facial palsy participated in the general recovery. After two weeks the effaced folds reappeared, largely restoring to the face its lost expression. The eye could be completely closed in three weeks. Drinking was soon no longer difficult owing to escape of fluids from the corner of the mouth. By the sixth week nearly all traces of the palsy were gone.

Examined three weeks after delivery the urine still showed some albumin, and does so to this day. We shall come back to this fact presently.

As will be granted, the case presents several noteworthy features. First, did the woman have syphilis? At no time were there any clear manifestations of the disease. This in itself is, however, no exceptional occurrence. Says Hutchinson: "Cases are innumerable in which a young wife remains in perfect health, never manifesting the slightest indication of disease, and yet bears an infant destined to show it." Such mothers, according to Colles' law, can suckle their syphilitic infants with impunity, while a healthy wet-nurse is in danger of infection. Some alleged exceptions to this law have been recorded and advanced in support of direct parental transmission with non-involvement of the mother. In the light of recent research,[1] however, Colles-Baumès' law appears to be *unexceptionally* valid, and the mother of a congenitally syphilitic infant is *without exception* and permanently immune against syphilis, not only of her own child, but against infection from any source whatever. Now, such a lasting immunity can be acquired, as in other infectious diseases, only by passing through an actual attack, since inheritance is able to confer no more than a transitory immunity,

[1] Rudolph Matzenauer. Wiener klinische Wochenschrift, February 12, 1903.

as plainly shown, for syphilis by authentic instances of *sub partu* infection (children infected with primary sores in passing through the genital tract of the mother). It would seem to follow, therefore, that every immune and apparently healthy mother has or has had latent syphilis. Such mothers not infrequently suffer at a later date from the tertiary manifestations, thus demonstrating *a posteriori* the correctness of the deduction. The important bearing of these considerations on prognosis and treatment is obvious. We may thus safely assume that our patient has passed through actual syphilis.

This inference is not without bearing on the nature of the facial paralysis in our case. Could the palsy have been luetic in origin? It involved both upper and lower peripheral branches. There was greater involvement of the lower, however. The affected eye could not be closed voluntarily without closing the other eye, while simultaneously with the latter its closure could be partially effected. The unaffected eye could be closed singly. This "sign of the orbicularis" has been looked upon by Board as pathognomonic of central paralysis, though Jacoby has found it present in peripheral palsies, and therefore inconclusive. W. M. Bechterew quite recently[1] has also observed the sign in peripheral facial palsies, but at a later stage, as a remnant of the affection. This illustrious author has demonstrated by experiments the value of the "orbicular sign" as pointing to a cortical or subcortical lesion. Winking in our patient was unaffected, both eyes participating in the act. Taste remained unimpaired.

In discussing the probable nature of the palsy, we must consider that slight hemorrhages into the retina and nose-bleed had occurred. Moreover, the time of appearance would rather lead to a non-specific explanation. The assumption seems to be most likely that a small central hemorrhage was responsible for the paralysis. Or, perhaps, the causative lesion was a localized œdema of the brain, as happens occasionally in uræmia. Finally, the palsy may have been purely toxic in character.

We now come to the most important aspect of our case, namely, the nature of the renal affection. Was it organic or was it functional? Did we deal with a genuine nephritis or with the so-called kidney of pregnancy?[2]

The existence of a nephritis antedating the last pregnancy is rendered unlikely by the anamnestic facts: not only were none of the corresponding complaints present, but the urine had been repeatedly examined by the attending physician and nothing disquieting had been found. It is thus safe to assume that the renal disturbance originated in the last pregnancy.

The kidney of pregnancy, according to Leyden, consists in anæmia of the organ with fatty infiltration of the renal epithelium, but without inflammatory changes. Attempts have been made to

[1] Obosrenie Psychiatrii, August, 1903.

[2] Schwangerschaftsniere Leyden.

account for this anæmia by the vascular constriction consequent on reflex irritation from the pelvic organs, by direct pressure of the uterus, by mechanical retention of urine, etc. There is a growing tendency, however, to attribute the renal changes during pregnancy (together with certain changes in the liver) to the action of toxic metabolic products, the accumulated waste matter of maternal and fetal metabolism. That toxic substances are often the cause of renal lesions is sufficiently well established, and, reasoning by analogy, it is easily conceivable how in pregnancy the metabolic poisons may inflict an injury on the renal tissues. At first the impairment may be slight, but prolonged action or great intensity of the poison is likely to result in more serious damage, which may finally culminate in a true nephritis. It is quite plausible, furthermore, that the auxiliary factors mentioned above contribute their share to the result, for there is no doubt that the toxæmia of pregnancy is a complex condition. The possible cumulative effect of repeated pregnancies may be a matter of etiological speculation, as may also in our case the antecedent syphilis and the mercurial injections.

With the removal of the causes the renal insufficiency of pregnancy would naturally tend to subside or disappear, as we actually observe in many such instances after delivery. When, however, the renal lesion has become more pronounced, it is perfectly comprehensible that it should persist after the primary cause has been removed. As a matter of fact, it has long been noted that genuine nephritis not infrequently becomes superimposed on the kidney of pregnancy. Even Leyden, who considers the renal disturbance as merely functional, holds this opinion. But here, as so often, no fixed line exists between functional and organic, the interval being filled up by intermediate transitional forms.

In our case the presence of such symptoms as retinitis and paralysis would point to a graver renal lesion and render the persistence of the latter after delivery highly probable *a priori*.

This conclusion has, in fact, been borne out by subsequent observation of the patient. At the time of writing, six months after delivery, the albuminuria still persists, and the urine contains morphotic constituents indicative of renal involvement. Occasionally œdema of the eyelids is noted in the morning, and the woman complains at times of headaches, gastric distress, etc.

In view of this and the empirical observation that successive pregnancies cause more extensive retinal degeneration, future conception in our patient will have to be prevented *a tout prix*.

ON THE OCCURRENCE OF CYSTIC CHANGES IN THE MALPIGHIAN BODIES ASSOCIATED WITH ATROPHY OF THE GLOMERULUS IN CHRONIC INTERSTITIAL NEPHRITIS.

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(From Prof. Chiari's Pathologico-anatomical Institute in Prague.)

During the past few years the Malpighian bodies of the kidney have been studied in greatest detail, not only in normal but also in diseased organs. Of the pathological changes, those associated with fibroid atrophy in chronic nephritis have, perhaps, been most thoroughly investigated. There is no doubt that this latter form of degeneration and atrophy of the glomerulus is well recognized, even though there are diverging views as to all the changes that precede the formation of the hyalofibroid spherical mass.

In the literature very little mention is found of another very frequent form of atrophy within the Malpighian body in the same disease, chronic interstitial nephritis, and it is to the histological pictures of this, as well as its relative frequency, that I hope to call attention in this paper.

In the literary synopsis which follows, it will be seen that the investigators of the early part of the second half of the last century, when thin sections and other refinements of technique were unknown, mentioned a cystic condition of the Malpighian bodies, whereas the recent writers ignore the condition. Rokitansky and Klebs, especially the latter, call attention to this in chronic interstitial nephritis, describing one phase of the change.

In the *Anatomie pathologique* (1879) of Laboulbène and in the *Histologie pathologique* of Cornil and Ranvier, published in 1884, the cysts that are found in chronic interstitial nephritis are discussed at some length. The frequent occurrence of these and their origin from uriniferous tubules they affirm, but they also mention as a rarity (Cornil and Ranvier) cystic developments from the Malpighian bodies in which the capillaries have almost entirely disappeared, just a few remaining attached somewhere along the wall of the cyst.

In the 1893 edition of Orth's *Special Pathology*, a cystic atrophy of the tubuli and Malpighian bodies in contracted kidneys and chronic interstitial nephritis is mentioned, but in the 1900 edition of his *Patholog. Anat. Diagnostik* he talks of these cysts as derived from tubules alone. Whether this is a change of view I do not know, but the fact that Baum, from Orth's laboratory, in 1900 published a paper in which he describes such a change in the Malpighian body as I am about to depict, and calls it a development anomaly or embryonic Malpighian body, suggests that in 1893

Orth's remarks were not intended to cover this peculiar pathological change, otherwise his pupil would have interpreted the picture in accordance with the earlier expressed views of Orth, or, at least, made some reference to the same.

In a picture in Dürck's *Atlas of General Pathological Histology*, p. 74, a cystic development from the Malpighian body is beautifully drawn. The lining membrane of the cyst is the typical wall of the Malpighian body—that is, Bowman's capsule—flat epithelium on a membrana propria; and at the right lower corner of the cyst are a few cells projecting into the lumen thereof, grouped irregularly about a bloodvessel. This cyst is filled with colloid, and is just the kind of cyst that is so commonly found in my researches. Dürck calls this a tubulus cyst. Otherwise little or no mention is found in reference to this change, except, perhaps, in Philippson's article (also in that of Beckmann), in which the former says he found hydrops of the Malpighian bodies similar to that seen in so-called congenital cystic kidney in kidneys of older people, but specifically states that there seems to be no relation between this and chronic interstitial nephritis (p. 556).

On the other hand, in Israel's (1889), Weichselbaum's (1892), Hamilton's (1894), Orth's (*Diagnostik*, 1900), Ribbert's (1901), Schmaus' (1901), Kaufmann's (1901), Ziegler's (1901), Langerhan's (1902), and Dürck's (1903) text-books the fibroid changes in the Malpighian bodies are discussed in more or less detail, but no mention of another—*i. e.*, cystic atrophy—is made. Weichselbaum, to be absolutely accurate, suggests such a possibility, while Ziegler and Ribbert mention the calcification in Malpighian body cysts that were described by Baum.

To avoid any mistake, I must mention here that the not uncommon macroscopic cysts lined with cuboidal epithelium, containing variously colored fluids and fluids of various consistency in chronic interstitial nephritis, are quite different from those to which I am about to call attention. These tubule cysts are very commonly visible to the naked eye, whereas the form that is derived from the Malpighian bodies is only occasionally so recognizable. If these latter are large enough to be seen by the naked eye, the microscopic examination alone can distinguish them from tubule cysts. Moreover, what I am describing has nothing to do with the small cysts that have been found in glomeruli that are undergoing the fibrohyaline atrophy. These "cysts" are minute spaces made by the irregular growth of tissue within Bowman's capsule and scarcely deserve the name cyst. They involve a small part of the whole Malpighian body and are only an indication of irregularity in growth of the newly forming intracapsular tissue (Engel, Tschistowitch).

Here it must also be mentioned that the cysts that I am calling attention to have been interpreted as tubule cysts by some authors

—*e. g.*, Dürck—as seen in the illustration referred to previously. Orth and Baum have expressed somewhat similar views, while Cornil and Ranvier talk of most of these same cysts as tubule cysts in which the epithelium has been flattened out. In single sections, where remnants of the glomerulus are usually not seen projecting into these cysts, this view of their origin might seem justifiable. It is probably due to this misinterpretation that we find so little mention of a second form of atrophy of the glomerular structures in medical literature.

From the foregoing it will be seen that more or less complete descriptions of four different kinds of cysts derived from the kidney parenchyma in chronic interstitial nephritis are found in the literature. Two are referred to the Malpighian bodies and two to the tubules. Of the former, one is scarcely a cyst, while the other, of which very little mention is found in the literature, deserves that appellation, but has never been studied and clearly described.

Of the *so-called tubule cysts*, the two varieties differ most markedly, according to Cornil and Ranvier, Orth, and Baum, not to mention others, in the nature of their epithelium; in one these cells are more or less high and cuboidal, whereas in the other they are completely flattened out against a membrana propria.

The studies that underlie this article are based on twelve kidneys of chronic interstitial nephritis which were examined in serial section and thirty kidneys in single section (*i. e.*, non-serially), to determine both the origin and the development of the cyst in question and also the frequency of their occurrence. The serial sections demonstrated the origin of a *large number of cysts, those with "flattened epithelium," from the Malpighian bodies, by showing atrophic glomerular structures adhering to the wall of the cysts, and the study of the single sections from the thirty kidneys with chronic interstitial nephritis showed that cystic atrophy is a very common occurrence.*

In the usual non-serial sections of kidneys in which chronic interstitial nephritis is found, one sees cystic spaces filled with a more or less homogeneous substance. The walls surrounding this substance are made up of two elements, a basement membrane and a layer of epithelial cells attached to it. In some of these the epithelium is flat, so that only here and there a nucleus, with a small amount of flattened protoplasm surrounding it, is visible; while in others, again, the epithelium is arranged as in the uriniferous tubules, the nuclei being near one another and the cells to which they belong being more or less cuboidal in shape. These two kinds of cysts impress one as very different structures. The wall of the former is identical in structure with that of the Malpighian bodies—Bowman's capsule—while the wall of the latter reminds one of the uriniferous tubules. In addition to these cysts, one occasionally sees an altogether different picture. One finds a cystic formation and projecting into the contents of the cyst (Figs. 1 and 2) are tufts

of capillaries, distinctly part of the glomerular tufts, but smaller in size than the normal capillary mass. The walls of these cysts are identical in structure with the walls of a normal Malpighian body, and, moreover, absolutely identical with the walls of the first of the above-described cysts—*i. e.*, flattened epithelium—whose nuclei are far apart (in usual sections), lying on a basement membrane.[1]

The size and general contour of these two "varieties" of cysts with walls of identical structure vary very much. In general, they are a little larger than the normal Malpighian bodies and more or less spherical. At times they are five to six times (in one plane) the size of the Malpighian bodies; at others even larger. They may be very irregular in shape, sending prolongations in between the tubules.

Of these two "varieties" the second is undoubtedly that to which Laboulbène, Cornil and Ranvier, and Baum refer, while the first is usually interpreted as a tubule cyst, despite the resemblance its walls bear to the normal Bowman's capsule and to the capsule of the cysts with small capillary glomerular tufts.

If these cysts that have been interpreted as tubule cysts with flattened epithelium are cut in serial section, in the majority of cases, one finds that at some spot attached to the wall and projecting into the lumen are some remnants of a glomerulus, very often one or more capillary vessels. In other words, those cysts with walls that resemble in their structure the walls of Malpighian bodies contain an atrophic glomerulus, so that in one or more sections one gets a picture such as the above authors have mentioned, while in all the other sections one gets the "variety" which has been interpreted as a tubule cyst with much flattened epithelium.

Having thus made clear the point that these cysts, so-called tubule cysts, are derived from the Malpighian bodies, I shall briefly point out the stages in this form of atrophy of the glomerulus, noting how both the capillaries and the visceral layer of Bowman's capsule behave in this process.

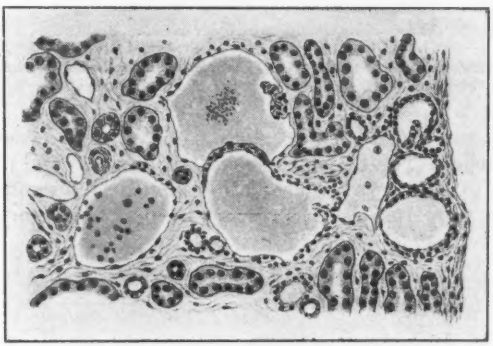
From a study of a great many sections in series, one can describe the various stages in this atrophy by a connected statement better than by describing in detail selected pictures. This I shall attempt in the following pages, repeating as little of what has been mentioned as accuracy will permit.

These cysts derived from the Malpighian bodies are, perhaps, most frequently found in the superficial cortical part of the kidney, and they vary, as just said, very much, both in their size and shape. They may be only slightly larger than a normal Malpighian body, but at times they are much larger and even visible to the naked eye. Their shape is most usually almost spherical, but it is not uncommon to find them very irregular in outline.

[1] As seen later other cysts of Malpighian origin show different remnants of the atrophying glomerular tufts, which are, however, rarely noted in non-serial sections.

The walls of the cysts are made up of flat epithelium lying on a basement membrane, absolutely identical with the structure of the normal Bowman's capsule. In serial section one finds any stage of atrophy between a fairly normal-looking capillary mass, smaller than the normal vascular tufts projecting into the cavity, to a single capillary vessel just projecting into the cavity of the cyst. At times not even this is seen, as detailed below. In the usual non-serial diagnostic section one more often finds no sign of the glomerulus, but occasionally, as in one of my specimens, one can see several cysts close together in one field (Fig. 1), in several of which one or two capillaries are visible. One can understand the whole process by finding these various stages in this atrophy of the capillaries from the cysts with fairly normal-looking capillary tufts of nearly normal size to those with only one or two vessels.

FIG. 1.



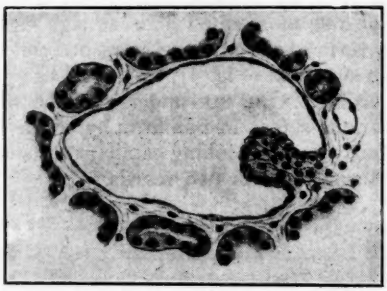
Shows directly under the kidney capsule three dilated tubules, and lying above these four Malpighian body cysts. Two of these show remnants of the glomerulus, the other two in this section show none. In two of the cysts, cells lie in the "colloid," in one fine granules of lime, and the fourth contains only the "colloid." (Drawn with 2 A. Zeiss.)

Rarer than these forms, of which the cyst with only a few vessels is the one most commonly seen in my serial sections, are those cysts that show no signs of glomerular vessels at all. Probably the relative frequency of one or the other stage of the atrophy in the glomerulus is dependent on the severity of the interstitial nephritis.

Not infrequently the visceral layer of Bowman's capsule, which now is fairly generally looked upon as a syncytium (Kölliker-Ebner), behaves in a very interesting way, which shows that the cells still retain individual characteristics, even if the theory of their syncytial life under normal conditions is true. In some of these Malpighian cysts in which the glomerular tufts are quite small, consisting of just a few capillaries, this visceral epithelial layer is very prominent, and

each cell is distinctly visible (Fig. 4), their outline being definite and clearly distinguishable. In other cysts, though the nuclei stand out close together, as in the fetal kidney, the cell limits are indistinct (Fig. 3). Moreover, many of these cysts, where little or nothing of

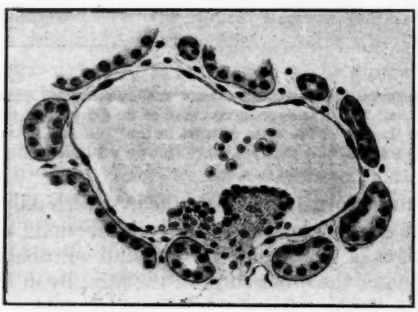
FIG. 2.



Shows similar cyst, but in this the cells of the syncytium have become individualized, each one being distinctly separable from its neighbors.

the capillaries remain, show small papillary excrescences covered with epithelium (Fig. 3), which, from their anatomy and the analogy they bear to other cysts, must be interpreted as a remnant of the syncytium supported on a tender branching framework of what

FIG. 3.

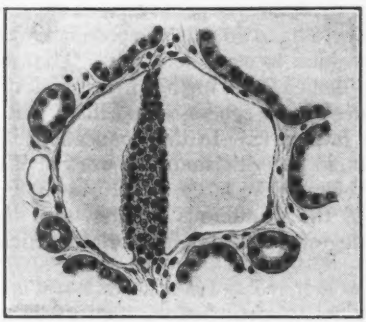


Shows similar cyst, in which the visceral layer of Bowman's capsule has become very prominent.

seems to be connective tissue. At times this more or less branched structure is attached to the cyst wall at both ends, dividing the cyst in some sections into two smaller cavities, which, however, communicate in the following sections of the series (Fig. 6).

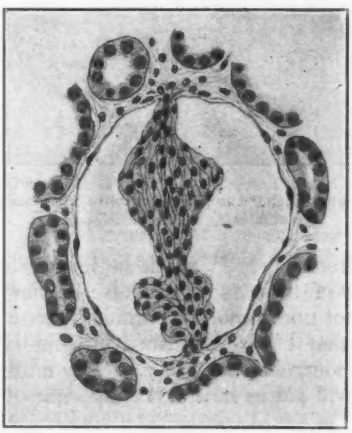
The origin of this dividing, incomplete septum or bridge is seen in the following process: occasionally the glomerular tufts (Fig. 5) become attached to the parietal portion of Bowman's capsule, more

FIG. 4.



Shows similar cyst, but here the capillaries have disappeared, and the proliferated visceral layer of Bowman's capsule has covered the bridge with epithelium.

FIG. 5.

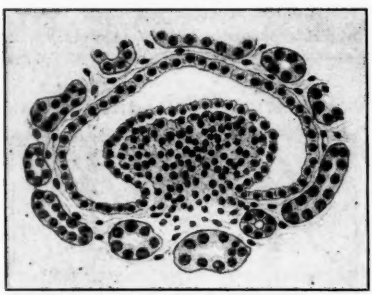


Shows another cyst in which the capillaries have become adherent opposite to the hilus. Pressure lines are distinctly visible running parallel from the hilus to the capsular adhesion.

or less opposite to the entrance of the artery of the glomerulus. The capillaries gradually undergo atrophy, so that in some pictures one can see a few capillaries running through the central part of the cyst, dividing it into seemingly two smaller cavities. With the

proliferation of the visceral layer of the capsule, when the capillary atrophy becomes extreme, a mass of epithelial cells, on a connective-tissue framework, is found running through the cyst, dividing it into two more or less equal parts (Fig. 6). Whether these papillary bodies and the rejuvenescence and proliferation of the epithelium of the visceral layer of Bowman's capsule, that were just described, have anything to do with the production of kidney tumors, I am not in a position to state definitely. That such a possibility exists cannot be denied, and further investigation must determine the relation between these processes and those that lead to tumor—*e. g.*, adenomata formation. In this connection, it is of interest to note that Grawitz, in his criticism of the work of Weichselbaum and Greenish, who referred the latter structures—*i. e.*, adenomata—to the epithelium of the uriniferous tubules, said that he had seen pictures which suggested a Malpighian origin. Ricker saw a similar

FIG. 6.



Shows a dilated tubule into which the growing connective tissue has pushed part of its wall, thus mimicking a Malpighian body cyst.

picture in an adrenal "rest," which he interpreted as a papillary growth. In view of these facts, and also in view of the fact that adenomata are not uncommon in chronic interstitial nephritis, this peculiar change that I have described in some of the Malpighian bodies that are undergoing the cystic atrophy must be kept in mind, and, perhaps, it will aid us in interpreting some of the new-growths of the kidney.

In all the cysts already described there is found some remnant of the glomerulus, but, in addition, one finds cysts of identical structure without any sign of the glomerulus projecting into their cavities. In these cysts the contents and the walls are of absolutely the same nature as those cysts which still show capillaries or the visceral layer of Bowman's capsule; and in single section the cysts that contain atrophic elements of the glomerulus and those that do not cannot be distinguished one from the other, unless the section happily strikes

the plane of the atrophying glomerular structures in the former variety of cysts. Even then only serial section will make sure that no glomerular elements persist in the second variety of the above cysts. This absolute identity in structure between the cysts that contain glomerular elements and those that do not leave no doubt as to their common origin from the Malpighian body. The absence of all glomerular elements may be the final stage in the atrophy of the glomerulus.

That this process of cystic atrophy does not seem to be due to inflammation within the Malpighian bodies must be emphasized. No signs of inflammation either in the capillary tufts nor in the parietal layer of Bowman's capsule were ever seen, except, perhaps, in that form of atrophy in which the capillaries had become adherent opposite to the hilus. No marked signs of inflammation between capillaries and Bowman's capsule were seen even here, but the adhesion probably owed its origin to some such process. All the other pictures—the usual ones—point rather to a mechanical factor without the Malpighian body as the direct cause of this condition of cystic atrophy.

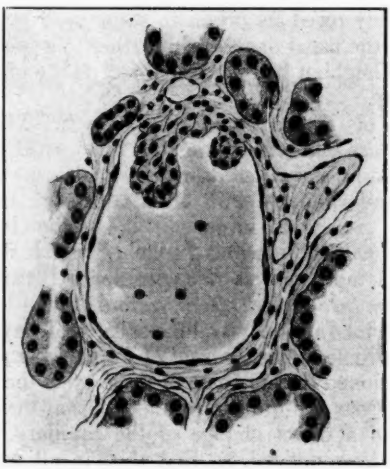
The contents of these cysts vary very much. The ground substance, if I may use that term, which fills them usually takes varying deep tints with eosin, stains yellow with Van Gieson, very faintly with hæmatoxylin, and similarly with alum cochineal, but still fainter after treatment with acids; in general, it has the characteristics of what is called "colloid." In this "colloid," which shrinks in hardening, leaving a more or less irregular space between it and the cyst walls, there are quite often various cells—leukocytes and epithelial—also not infrequently lime-salts, as I have described in another recent article in the *Journal of Pathology and Bacteriology*. It must be mentioned that in some of these cysts the fluid does not stain, but such cysts are quite rare and unusual in my experience. No indication of a direct change of the capillary tufts into this "colloid" were ever noticed, so that this, in all probability, is a product of secretion rather than a degeneration of previously normal protoplasm.

In looking for a tubulus contortus in connection with these cysts, it was the rule not to find any. Practically all of the cysts were blind, and this probably helps to explain their origin. Somewhat similar cystic Malpighian bodies are seen in congenital cystic kidneys without the "colloid" contents, and from the similarity in the picture and the fact that the tubuli contorti seem to be usually shut off, I think we can assume that the Malpighian body cysts in chronic interstitial nephritis owe their origin to a similar mechanical process, to obstruction in the efferent uriniferous tubule. Whether the very few cysts into which a tubulus contortus could be traced owed their origin to an obliteration or stenosis of this tubule some short distance from the Malpighian body, instead of directly at its origin from this

body, I cannot state definitely. Perhaps, even in these there was a stricture at the insertion of the tubule into Bowman's capsule. It is of importance to note that where I found a tubulus contortus opening into a cystic Malpighian body, which in all my specimens I saw only a few times, the Malpighian body cyst was about the size of a normal Malpighian body.

What the nature of the process that leads to obstruction in the tubule is we can only guess at for the present, as it is almost impossible to imagine a method of investigating a stenosis of these channels. One would naturally think of the new connective tissue and its subsequent contraction, which is so characteristic of this form of nephritis, as the cause. It is of importance to state that I did not

FIG. 7.



Shows Malpighian cyst with atrophic glomerulus flattened more or less against the cyst wall. Capillaries are still present. Contents of this cyst, cells and "colloid." (Figs. 2 to 7 drawn with 2 D. Zeiss.)

find any irregularity in the presence of new connective tissue about or near the cysts, but it seems likely that contracting bands at some distance might lead to occlusion of the tubuli contorti without being necessarily in absolute proximity to those tubules. Another method of closure might be within the tubule itself, as mentioned above, due to stricture formation. Perhaps future investigation will make these points clear.

Before leaving this general description I must state that although the signs of increased pressure within the Malpighian bodies were present in many instances they were scarcely the rule. In some

cysts the remnants of the capillaries were spread out along one side of the wall, as if pressed and flattened there (Fig. 2). In the cases where adhesions had formed between capillaries and parietal layer of Bowman's capsule opposite to the hilus, the signs of pressure were even more distinct (Fig. 5); and the capillaries ran almost parallel to each other, being pressed together from the sides. The increase in size of the Malpighian bodies undergoing this cystic change and the frequent cystic prolongations between the tubules are also indications of a heightened pressure, as no signs of active proliferation of the capsule were visible in any case. That the increase of internal pressure must be very gradual in these closed-off Malpighian bodies is evidenced by the fact that most of the glomeruli undergoing this atrophy show no signs of active pressure in their general conformation.

From all the above it will be seen that in chronic interstitial nephritis the Malpighian body undergoes a change which is quite the opposite of the usually described "fibrohyalinization." This latter change most often depends on a vascular disturbance and leads to shrinkage of the whole structure, while the former, the cystic atrophy or degeneration, probably depends on a disturbance in the efferent uriniferous tubules, and leads to the formation of a cyst somewhat or much larger than the original Malpighian body. Both have in common the more or less complete destruction of the glomerulus.

As to the frequency of occurrence of cystic atrophy of the Malpighian bodies, the following table, based on sections from thirty different cases of chronic interstitial nephritis, will show. In each case one section was gone over and both fibroid and cystic Malpighian bodies were counted and arranged in parallel columns:

THIRTY CASES OF CHRONIC INTERSTITIAL NEPHRITIS WITH ENUMERATION OF GLOMERULAR CHANGES.

Cases.	Cystic atrophy.	Fibrohyaline atrophy.
1	8	3
2	3	2
3	10	7
4	4	3
5	0	2
6	3	4
7 in infarcted area	0	81
7 in non-infarcted	4	1
8	2	1
9	4	1
10	0	2
11	2	1
12	1	1
13	8	8
14	0	9
15	4	0
16	2	2
17	1	13
18	2	1
19	1	3
20	2	0
21	0	2
22	0	5
23	1	0
24	0	2
25	2	3
26	6	0
27	3	3
28	1	3
29	2	2
30	3	4
Totals	79	169
Exclusive of infarcted area	0	81
	79	88

It will be seen that these two changes are almost equally frequently seen if we exclude the areas where infarcts appeared in the sections, for here the vascular change was the direct cause in the overproduction of the fibroid atrophy. But even if all these areas are included in our estimate, the proportion of cystic to fibroid changes is surely a large one and well deserving of more attention than it has received.

Looking a little more closely at these figures, it is evident that in these thirty single sections 248 atrophic Malpighian bodies were found. Of this total 79 were cystic and 169 were changed into the well-known fibrohyaline masses. Expressed in percentages, 31 per cent. were cystically changed, whereas the rest had undergone fibrous atrophy. If those sections in which no infarcts were noted were considered alone the percentage of cystic to fibrous would be considerably changed. From this point of view, 47 per cent. would be cystic and 53 per cent. fibrous atrophy.

It is also evident that in some sections no representatives of one of the two pathological changes may be found, and in other sections one form is more frequently seen than the other. A similar table could be made from the kidneys that were cut in serial section, and this emphasizes the fact that the above enumeration from single sections is absolutely reliable.

In closing, I wish to emphasize the two most important facts that have been brought out in the preceding pages:

1. In addition to the well-known fibroid atrophy of the Malpighian body in chronic interstitial nephritis there is also a cystic atrophy.

2. Cystic atrophy is very common and in my cases almost as frequently seen as the fibroid change.

In closing, I wish to thank Professor Chiari for the material on which this work is based and for his many kindnesses while studying in his laboratory.

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A PARTIAL STUDY OF ULCERATIVE ENDOCARDITIS.

By Beverley Robinson, M.D.,
of new york.

The subject of ulcerative endocarditis formed the thesis of Dr. Osler's Goulstonian Lectures in 1885. He begins them as follows:

"It is of use, from time to time, to take stock, so to speak, of our knowledge of a particular disease, to see exactly where we stand in regard to it, to inquire to what conclusions the accumulated facts seem to point, and to ascertain in what direction we may look for fruitful investigations in the future." [1]

It is with this spirit I have undertaken a renewed study of ulcerative endocarditis.

In 1898 Sir Douglas Powell delivered before the Royal College of Physicians of London "Lectures on the Principles which Govern Treatment in Diseases and Disorders of the Heart." [2]

In this third lecture he carefully considered those which specially dominate the treatment of ulcerative endocarditis. There he also reviewed the therapeutic measures likely to be of some use in the disease. He likewise gave a tabulated statement of the results of treatment by antistreptococcic serum, and of his own experience with yeast and with nuclein, after the method of Dr. V. C. Vaughn, of Michigan. In the Lumleian Lectures during the current year, Dr. T. R. Glynn[3] has again reviewed this subject and regarded it "mainly in its clinical aspects." He was influenced to do so because of its great clinical interest, and the fact that no disease presents itself under a greater variety and perplexity of forms. A very elaborate historic retrospect of our growing knowledge pertaining to the disease is at first dwelt upon. In it he cites Matthew Bailey, Morgagni, Senac, Corvisart, and Bouillaud. To the latter he ascribes the honor of associating ulceration of the cardiac valves with symptoms of typhoid fever. He shows how the "third period" was marked by a perfected bacteriological technique, and by the fuller comprehension of the biological characteristics of bacteria. Thus ulcerative endocarditis, which was formerly considered as a local affection, is now regarded as one of the complications of a general infection.

This malady, like the simple form of endocarditis, affects the lining membrane of the heart and especially the nerves. It is characterized by vegetations and is accompanied with loss of tissue. The ulceration may cause perforation of heart valves, or even of the septum or heart walls, under very exceptional conditions. With the ulceration we may find a limited area of suppuration. It is very rarely a primary affection, but ordinarily occurs as a

complication of some infective disorder, or septic disease. No doubt this view explains how it is that the lesions of simple endocarditis often precede and are found in conjunction with those of the more advanced or far graver form of the disease. Between the latter and the benign malady there is, indeed, no essential anatomical difference, and they merely represent gradations, as it were, of more or less intensity.

Although cases which have developed primarily are occasionally observed, they are so infrequent as to have had legitimate doubt thrown on them. Osler reports one case in which at the autopsy no lesions were found other than those of ulcerative endocarditis.[4] In cases of obscure origin it is probable that the micro-organisms frequently enter the economy by the respiratory passages, and reach the heart in this way rather than through the digestive organs. Especially in cases of chronic heart trouble by reason of secondary congestion of the air-passages, the conditions become favorable to bacterial invasion. An infective endocarditis originating in this way would occasionally appear to be of primary origin. (Glynn.)

On the other hand, ulcerative endocarditis occurs quite frequently as a complication of pneumonia. "In 16 cases of 100 autopsies in which this lesion was present, 11 were of this form."[5] According to Wells, the proportion in all cases of pneumonia is 3 per cent., while the percentage in fatal cases of the latter disease is 4 per cent. G. Studa's estimate of the relative frequency of ulcerative endocarditis in pneumonia is a much higher one (9 cases in 85 autopsies).[6] When it is found in this disease it appears to be exceptionally virulent, as numerous autopsies demonstrate. It is also seen in acute rheumatism. Anders[7] writes that the proportion is about 10 per cent. of the cases in which acute endocarditis appears. It may also occur as a complication of some eruptive fevers and in septicæmia. Vaccination has been followed by cellulitis and infective endocarditis. (Coleman.)

Cases are likewise due to dental caries and oral sepsis. When we consider the great number of cases of acute and subacute rheumatism we are called to treat, the number of those complicated with ulcerative endocarditis seems very small.

Ulcerative endocarditis often follows septicæmia of various origin, and is not uncommon in gonorrhœa. The intimate relations between some cases of gonorrhœa and ulcerative endocarditis have been established for more than twenty years, but it is only lately that these instances have been studied in a systematic manner.[8] A fatal case of this kind has been reported.[9] In some of these cases it has been impossible from the most careful local researches to discover the site of entrance of the infective disease. We should then turn to cultures made from the blood, and occasionally bacteria with the typical characteristics of gonococci will be shown.[10]

The cultivation should be made during life, and it may be con-

firmed at the autopsy from blood taken from the heart, or from the cardiac vegetations. For the cultivation it is not essential to take a great deal of blood, to dilute it much, or to make use of special media. It is now known, also, that the bactericidal action of the blood is less pronounced on gonococci than it is on pneumococci or the typhoid bacillus. The septic process that proceeds from the puerperal state is also a well-known source of grave ulcerative endocarditis. Although certain authors have described it as a complication of malaria, it is questionable whether such cases often occur. Among diseases which are occasionally complicated with malignant endocarditis I would cite measles, scarlatina, smallpox, erysipelas, and typhoid fever. In my experience such instances, with the exception of the latter disease, have not been seen, and even of this finding I have no available record.[11]

Cerebral complications are associated with it at times, particularly, as meningitis,[12] and this is especially true when the malignant endocarditis is found with pneumonia. I have observed one case of obscure mental disorder in which the malignant endocarditis was shown to be "mural" at the autopsy, and no gross changes had taken place in the brain. Miliary abscesses have been found, however, in a number of instances. Once Jackson found an embolus of the artery of the Sylvian fossa, and Lartigau[13] reports a case of gonorrhœal origin, in which prior to death there was a sudden aphasic attack. The bacillus of influenza has also been detected in the valvular vegetations of ulcerative endocarditis. The cases observed were instances of the development of the disease upon a chronic cardiac affection.[14]

This fact is important as pointing to a demonstration of what has long been considered probable, namely, the vulnerability of the heart to the influenza poison. Ulcerative endocarditis occurred in 4 of de Batz's 20 cases, and a most interesting example has been recorded by Tickell. It has been observed during the influenzal attack, but most frequently in the convalescing period.[15]

A new organism of endocarditis, called micrococcus zymogenes, has lately been pointed out in a patient who died. The infarcts which accompanied this case are not stated to be other than bland; therefore it may be that the endocarditis itself belonged to the simple type. On the other hand, Maccullum and Hastings report a case caused by this organism, in which multiple septic infarctions in various viscera were found. Further, typical acute vegetative endocarditis was experimentally produced by intravenous inoculation in a rabbit and a dog, and the cocci were demonstrated in pure culture in the vegetations and in other parts of these animals after death. The micrococcus zymogenes is stated to be extremely minute, often elliptic in outline, usually found in pairs, is not motile, and stains with the ordinary stains.[16]

Although it is stated by some writers that the two forms of the

disease, simple and ulcerative, never become one and the same, this affirmation is probably too positive. Litten believes that prompt response to the salicylates is characteristic of the benign form.[17] They may be used, therefore, with some measure of reliance to determine an otherwise doubtful diagnosis. Litten also criticises Lenhartz's views as to the fact that the finding of micro-organisms in the blood characterizes the endocarditis as septic. Very justly he remarks that if later the microbe of acute rheumatism be accurately determined, such distinction will be no basis to rest upon. In the septic-malignant form of Litten, suppuration occurs in thrombi and joints, which does not occur in the non-septic malignant form. He objects strongly to the term "ulcerative" endocarditis, but does not believe the time has come to make separations on the ground of the presence or differences of micro-organisms. Poynton and Paine consider that ulcerative and other forms are only different degrees of the same disease, and that benign forms may become malignant under the "influence of virulent breeds" of the common micro-organism of rheumatism. Ewart insists that, even though the practical identity of the organisms may not be proven, a very important clinical lesson is furnished. This essentially means that our efforts of prophylaxis in rheumatism should be strengthened, because in prophylaxis of this disease we also combat the development of most serious cardiac affections.[18] An equally important matter has already been insisted upon by Sir Douglas Powell in his Lumleian Lectures where he directs "attention to the necessity of observing certain prophylactic precautions during convalescence in rheumatic endocarditis" (*loc. cit.*, p. 1153). The lesions found may be in the heart, or other organs of the economy.

In Jackson's cases enlargement of the spleen was present in all but one instance. Leukocytosis was also regularly found, the leukocytes usually numbering from 16,000 to 20,000. This is an important point in the differential diagnosis from malaria, tuberculosis, and typhoid fever. The bacteria in the blood are important and have different forms. In 23 cases studied bacteriologically by Jackson "in 2 no cultures were obtained; in 2 there were micro-organisms which were not identified; in 8 streptococcus pyogenes was found; in 5, the pneumococcus; in 3, staphylococcus aureus; in 1, the colon bacillus; in 1, the streptococcus and staphylococcus; and in 1, the streptococcus with other organisms."

In the 38 cases discussed by Lenhartz, the author carried out bacteriological investigations in 28 cases. In 16 cases bacteria were found during life. They were principally staphylococci. According to Lenhartz it is usually comparatively easy to find the organism in the blood.[19] From the point of view of prognosis it is very desirable to differentiate between the various forms of ulcerative endocarditis. This may be accomplished by careful blood cultures during life. It is especially desirable at present, by reason of the more

hopeful outlook of these cases. This seems to be proven partly by the results from treatment, partly by the data afforded by careful autopsies. Ewart, indeed, has stated, even in cases that resulted fatally, that evidences of repair in the local cardiac lesions could be shown. It may be remarked that there is little tendency in this process toward *cicatrization*, so that recovery may take place with little or no deformity of valves or orifices. (Wells.) The cardiac changes will depend upon the nature of the organisms which occasion them, and also upon the extent and duration of the disease. We do not find the same conditions in instances in which the process is wholly acute, and those where the acute disease is attached to former sclerotic changes of the valves. Usually we find vegetations on the valves. These are often found with an ulcerative process and small abscesses. According to Wells the distinguishing features of them are their massive character and broad base. Moreover, they do not extend often beyond the valves. The left heart is more frequently the site of the disease than the right. In regard to this point errors may be found in literature. Still the right heart is attacked oftener than in the benign form.

Mural ulcerative endocarditis is extremely rare. I have seen only one case, to which I have referred. The history of another one, hitherto unpublished, has been kindly given to me by my colleague, Dr. Van Horne Norrie. In rare instances the process may extend to the aorta and pulmonary artery. A secondary infective arteritis in various peripheral situations and in the different viscera, as a result of septic embolism from the heart, may also occur.[20] The vegetations are frequently small, especially when they alone are present. They are of gray or yellow color, and are situated on the margin or at the base of the valves. Under the microscope they are shown to be composed of numerous microbes, embryonic cells, and leukocytes. They also contain fibrin.[21] In many instances, however, the vegetations are larger and may become pedunculated. They have a markedly gray aspect also, or are covered with blood clot, and often show superficial or deep ulceration of tissue. In the latter case an aneurysmal pouch may be found. This pouch formation doubtless is due to blood pressure upon softened and degenerated valvular tissues. Sometimes the ulceration goes deep enough to make a perforation of the valve. Again, it extends to the chordæ tendineæ, beginning in the inflammatory stage, and separates later the valve segment completely. When this takes place we may have a flapping with each ventricular contraction of the detached valve against the auricle. Thus, secondary infection of the auricular walls is produced, and it is not uncommon to find warty growths here situated. In rare instances when the ulceration has enlarged and become still deeper, the septum or ventricular walls may be perforated. If the malignant endocarditis be caused by pyogenetic organisms it is not uncommon to find small abscesses in the valves,

or, indeed, in other parts of the heart. These abscesses may rupture, sometimes with perforation of the heart walls, and then pus is found in the pericardial sac. It is also possible for small quantities of pus to be reabsorbed, and the evidence of this is found in old scar tissue, or calcareous deposits. In some cases, especially when malignant endocarditis is found in a patient suffering from chronic heart disease, the vegetations may be capped with calcareous incrustations. In very rare instances the deposit of lime salts may occur in acute cases.

The ulcerative condition of malignant endocarditis may possibly be confounded with that which follows the necrosis of former atheromatous deposits, or those incident to chronic rheumatic endocarditis of benign nature. A differential diagnosis may here be made, probably with the use of the microscope; but at times doubt may still remain. Osler, in an analysis of 209 cases, showed the proportion in which the different valves, the walls, and sides of the heart are involved. His report reads "aortic and mitral valves together, 41; aortic valves alone, 53; mitral valves alone, 77; tricuspid in 19; pulmonary valves in 15, and the heart wall in 33 instances. In 9 instances the right heart alone was involved; in most cases, the auriculoventricular valves." [22] In Strada's 85 autopsies the seat of the affection was in the left side of the heart alone in 6 cases, and in the right alone in 3 cases. In Jackson's 43 examinations post-mortem we find that "the aortic valves were affected in 9 instances; the mitral, in 15; both, in 10. The right side of the heart was involved 6 times, and the endocardium of the ventricle 3 times. In 5 of the aortic cases there was old endocarditis; it was present in 7 of the mitral cases. The malignant disease had become implanted upon the old disease."

The mechanical factor, however, is not considered essential by Lenhartz, and he has shown that fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present. In Glynn's cases "the infective endocardial lesions were distributed as follows: the aortic and mitral valves were involved in 21 cases, the aortic in 10, the mitral in 15, and the endocardium of the ventricle alone in 1. The right side of the heart was involved in 6 instances" (*loc. cit.*, p. 1073.) Mural endocarditis is apt to affect either the upper portion of the septum of the left ventricle or the posterior wall of the left auricle.

According to the analysis of Kantback and Tickell, in 84 cases there were 51 males and 33 females; and in all but 16 cases old cardiac lesions were found. (Allbutt, p. 877.[23]) In Glynn's cases he found 65 per cent. of patients were males and 34 per cent. were females—"figures approximating those of Dr. Osler." The disease occurred, however, more frequently in young women than in young men. It was also remarked that the disease was likely to occur under conditions attended with general debility. In only

7 per cent. of the cases had an inflammation of the lungs preceded the endocarditis; in 11 per cent. of his cases the endocarditis originated in a recognized infective focus. The vegetations may become detached in larger or smaller masses and, carried by the circulation, form embolic plugs in different organs. Notably we find the kidneys and spleen affected; less frequently the brain and intestines are involved. The place where the embolic mass is arrested depends largely upon its size. While small emboli are more apt to be seen, it is not unknown to have a large artery completely obstructed. If the lungs contain infarcts, the embolic plugs originated in malignant endocarditis affecting the right heart. The embolic plugs are more or less numerous. In some cases where the malignant endocarditis is very pronounced and the ulcerative condition extensive, the autopsy does not show any embolic processes in the organs. They are also more or less irritating.

Consequent upon the degree of their infective nature follows the rapidity with which abscesses are formed. At the site of these abscesses it is not uncommon to find the arterial vessel already softened and ulcerated. Very many small abscesses are found at times in different organs of the body. Sometimes hemorrhage may be combined with the abscesses. Why in some cases the one is more frequent than the other is not positively known. (Strümpell, *Practice of Medicine*, 1901, p. 306.) Embolism was found to be "nearly three times as frequent in the infective as in the simple cases." (Glynn, p. 1076.) It is noted, contrary to the usually accepted opinion, that the so-called infarcts are not due to embolism, but are the result of "apoplexies" following the rupture of small bloodvessels, and made "specially liable to occur in severe passive congestion of the lungs."

The micro-organisms found in malignant endocarditis are pneumococci, streptococci, staphylococcus pyogenes aureus and albus, the gonococcus, and other organisms. The former are most frequently concerned, either alone or associated with others. The pneumococcus infection is more frequent in aortic endocarditis, the streptococcus infection in mitral endocarditis.[24] While in septic diseases malignant endocarditis is prone to occur, there are cases in which the valves are but slightly involved. In no case does the endocarditis form more than a part of the general septic condition. If, however, the heart is notably affected, it hastens very much the spread of the poison, and thus this organ becomes very important in the estimate of the gravity of the case. Of course, there is in these cases the local disease of which the malignant endocarditis is the result. This may be of the nature of an acute necrosis, a wound abscess, or puerperal disease, when there may be primary septic foci in the uterus, or its adnexa.

The etiology of the disease is varied. This is known. Many cases follow an infectious disease, especially pneumonia. This fact

has been pointed out by Osler. Still there are cases which appear to be primary (Jackson), as no assignable or sufficient cause of their development can be discovered. All forms of endocarditis, whether ulcerative or benign, seem, according to later investigations, to be of parasitic origin.* This view had been entertained also by Bartel. According to this author, in cases of rheumatic origin the organisms soon die, and often are not discoverable, particularly in cases which have run a somewhat chronic course. There are, however, some cases which "are apparently not due to the direct action of micro-organisms." These are caused by thrombotic deposits, and are possibly the results of the action of bacterial toxins.†

In a peculiar case of endocarditis reported by Hopkins and Weir, in which death resulted from cerebral hemorrhage, we have one that "seems to belong to the group on the border-land between a septic and ulcerative endocarditis; all the emboli were simple, not septic."‡

Thayer and Lazear[25] have gone thoroughly into the subject of gonorrhœa as a cause of septicæmia and ulcerative endocarditis. In their paper they show that the discovery of the gonococci in the circulating blood and upon the cardiac vegetations was made by Blum in 1895. The endocardium may be directly attacked by the gonococcus, as the general infection may be the immediate cause of the local trouble.

Ulcerative endocarditis is a rare disease in childhood. When it does occur in childhood it does not differ essentially from the disease in the adult. One case is reported in an infant ten months old, by L. D'Astros,[26] which resulted fatally. This case followed diphtheria, and, as was shown at the autopsy, was the result of a staphylococcus infection. Cultures from the heart gave a pure growth of cocci. Holt[27] reports a case from Harris in a child four years of age. The lesion in this instance affected the right side of the heart and was secondary to a cardiac malformation. Another fatal case in a girl fifteen years old is described by Cantley. In this case the pulmonary valve was affected. On the other hand, Adams relates a case of recovery as one of only four hitherto reported under the age of fourteen years.§ The greater proportion of cases reported in early life have been over ten years of age. There are 25 or more of these (Holt), and although the right heart is occasionally affected, the disease, according to Lannois and Paris, seems usually to attack the aortic valves.[28] Loeb describes such a case where there were extensive lesions of this valve, and which followed gonorrhœa. The diplococci found had the morphological appearance of gonococci.

* Poynton and Paine. Medical and Surgical Society of London, April 8, 1902.
† Year Book, loc. cit. ‡ British Medical Journal, June 13, 1903, p. 1373.
§ Archives of Pediatrics, December, 1902.

While the authoritative cases of ulcerative endocarditis of rheumatic origin are infrequent, such cases are occasionally described. E. Berie[29] reports two such. The bacillus coli is rarely found and seldom exists as a cause. Still, cases are described both by Henchen and by Andrews.

The symptoms of malignant endocarditis vary very much in individual cases. Sometimes the signs pointing to endocarditis are very indistinct, or entirely absent. This is true particularly where the cardiac disease complicates another acute infectious and septic disease like pneumonia, empyema, or meningitis. Herzog, O'Donovan, and others report cases which appear to support this position. Not only is the difficulty of recognition very great by reason of the absence of distinctive signs, but also by the variety of clinical symptoms present. The latency of the disease is sometimes such that a diagnosis cannot be made in the beginning.* Gavala's case is an instance of this sort. In many cases during life there are no cardiac murmurs, and the diagnosis must be based wholly upon the symptoms.† Again, the symptoms may be most misleading and point to a very different disease, as in the two remarkable cases of N. Pitt,[30] in which symptoms at first appeared to be those of spinal disease. The complete absence of fever also in a given case is not an absolute reason for calling in question the diagnosis, as witness the fatal one reported by C. O'Donovan, without fever.[31] In very few cases of Glynn's patients were there rigors, and in some pyrexia was absent for days and weeks at a time. It may be remarked that the former part of this experience is certainly almost unique. The difficulties attending the diagnosis are sometimes insuperable, for trustworthy clinical indications may be wanting. (Glynn.)

In other instances where the malignant endocarditis is subacute or chronic, and complicates an endocarditis of rheumatic origin, it may show distinct signs and is quite easily recognized. In the former cases the autopsy alone reveals the nature of the disease.

Occasionally the differential diagnosis between rheumatic and acute infective endocarditis is practically almost impossible. There is a mild form of malignant, non-septic endocarditis which resembles in many particulars the grave form of septic endocarditis.‡ In this form, while the local symptoms are not dissimilar to those of simple endocarditis, the general condition is notably bad. In this form we have hemorrhages of the skin and mucous membranes, and emboli in various organs, and also joint implications. But though the joints are swollen and tender the inflammatory arthritis remains serous; it does not become purulent. In the graver cases of this type the patient will often succumb after a few weeks' illness to an aggravation of the general condition. On the other hand, the milder cases will often recover.[32] The severe malignant form of

* Jackson, loc. cit.

† British Medical Journal, May 19, 1900.

‡ Strümpell, p. 307.

endocarditis is almost invariably of septic origin. It is of distinct etiological origin as compared with the milder form referred to. It is characterized apart from cardiac symptoms by the formation of metastatic abscesses in different organs, with or without the accompaniment of hemorrhages. The malignant endocarditis and the metastatic abscesses are directly referable to micrococci; the parenchymatous swelling and changes of organs are the result of the transport of toxins. The microscopic investigation of the different organs often shows the march of the pathological process and how it originated in small foci where minute vessels are filled with micrococci, which later produce areas of cell necrosis, finally leading to suppuration. Because at times no origin at all is discoverable for this form of disease, it seems very obscure. Again, the disease is occasionally not seen by the physician until its later stages, and hence its diagnosis is rendered even more difficult. Very often a pronounced leukocytosis will help us recognize the disease, but the feature of greatest significance is the finding of micrococci in the blood during life. This has already been accomplished more than once. Further bacteriological investigations in this direction are most desirable. Some of these cases run a very chronic course, and one case is reported by Osler where the disease lasted over a year. The autopsy showed extensive vegetations and ulceration of the mitral valve (p. 704). The fever is not always remittent; it may be high and continuous. The rashes, under certain circumstances, may render the disease liable to be confounded with typhoid fever or cerebrospinal meningitis. The sweating is often most profuse. Jaundice is occasionally present and may render confusion with acute yellow atrophy of the liver possible. Cases, even the most acute, usually last a week or more, and yet the disease has been known to terminate fatally in forty-eight hours.

Ordinarily, malignant endocarditis is an intercurrent or secondary affection of some primary septic process. The symptoms of this primary state should not therefore be confounded with those belonging to one of its localizations. It is, however, frequently most difficult to differentiate them. Many of the febrile attacks, which occur in cases of chronic endocarditis and which are accompanied with grave symptoms, result in ultimate recovery. It is very difficult in these instances to be sure whether these cases belong to the benign or malignant variety of ulcerative endocarditis during the period of the acute attack. The fact of the recovery, of course, argues strongly in favor of the benign form, although the clinical symptoms closely simulate those of the graver disease.

As to whether an acute endocarditis will be simple or ulcerative may depend somewhat upon the number or nature of the bacteria transported by the blood. Yet as we find the same bacteria in both forms of disease, this position is not wholly tenable. It seems probable that the particular outcome locally, of the fixation of the

bacteria, will depend more upon their virulence than any other one factor. It is also true that ulcerative endocarditis is liable to attack those persons suffering from exhausting diseases and the different cachexiæ. In some cases of ulcerative endocarditis the diagnosis is based mainly on the septic symptoms, and there is little or nothing in the local examination of the heart which will throw light on the case. On the other hand, a suddenly developed cardiac murmur, or a distinct and rapid modification of one already existing and showing previous valvular disease, will have great importance in diagnosis. It is necessary, therefore, in all suspicious cases, to make frequent and careful examinations of the heart, and to note all changes of rhythm which occur. The same is also true of the timbre of the murmur which may change at any time, and from being harsh and loud from the previous lesion may become soft and blowing by reason of the fresh disease which has developed. Combined with the heart symptoms are those of sepsis and embolism. The presence of fever and the numerous petechiæ or hemorrhages are always very significant; these symptoms being rarely combined in ordinary rheumatic endocarditis, sometimes the discovery of some evident cause of the septicæmia will bring light to an otherwise obscure case. Thus a foul vaginal discharge, which may be the result of an abortion in which the neck of the uterus has become abraded, will in this way prove satisfactory.

While chills, fever, and sweating point to septic fever, they do not fix the diagnosis of ulcerative endocarditis, and this must be done by examination of, and findings in the heart, or else by the changes due to emboli in the organs. Skin, urine, spleen must be frequently examined with this end in view. When other means fail to establish a diagnosis, an examination of the blood should be made. It is claimed that in most infections there is a decided leukocytosis, but in ulcerative endocarditis this statement is not always correct, according to Neussen, who says there is either an absence or possible decrease of leukocytosis.* On the other hand, Kelly dwells upon the importance in diagnosis of the presence of a moderate leukocytosis of the polynuclear variety. The latter also insists on the positive result of bacterioscopy of the blood. Likewise he attributes much value to the fact of the great instability of heart action, which may be noted in a very brief period. Some cases of ulcerative endocarditis may be readily mistaken for typhoid fever. In the latter, even though of severe type, hemorrhages in the skin are very rare. Moreover, we have earlier enlargement of the spleen, and pronounced abdominal symptoms, usually like tympanites, diarrhœa, distention, and rose spots. In all doubtful cases we should make the Widal test, and sooner or later we expect to get it in typhoid fever. The presence of this test would also help to

* Babcock. Diseases of the Heart, p. 181.

eliminate acute miliary tuberculosis, with which ulcerative endocarditis might be confounded. Unfortunately, the Widal test is not always absolutely reliable, even when present, to determine the differential diagnosis. One such instance is reported by Mathews and Moir,* where the Widal test was positive, thus confusing the diagnosis with one of typhoid fever. The autopsy showed that the disease was one of ulcerative endocarditis. Some instances, also, are reported, where the Widal test has proved negative. In other cases there has been a positive Widal reaction, and with different strains from one in twenty to one in two hundred. We thus perceive that this reaction is incapable at times of differentiating between these cases.†[33] The serum reaction in the differential diagnosis may be misleading in other instances, notably in septicæmia and acute tuberculosis. (Glynn.) Acute miliary tuberculosis may be differentiated frequently by the presence of tubercle bacilli in the sputum, and also by the preponderance of chest signs over those indicating a heart lesion.‡ I have had one case, unfortunately, of miliary tuberculosis of the lungs under my care, which resulted fatally, in which no tubercle bacilli were ever found, and in which the chest signs were changeable and uncertain for several weeks. In this case there was a soft, blowing murmur at the mitral orifice. There were, however, no hemorrhages of the skin, and no manifest symptoms pointing to emboli in the viscera. At one time there was slight hæmaturia, which made me somewhat suspicious of the renal condition. In a few days this cleared up, and I thought it was explained by renal hyperæmia, due to the febrile nature of the disease. The recurring chilly sensations, profuse sweats, and dyspnœa may occur in both diseases. The loss of flesh and strength may also be marked in both.

The temperature chart is probably more irregular and different in ulcerative endocarditis. Here again I have found it very difficult at times to pronounce in which direction I was carried by its careful consideration. As a rule ulcerative endocarditis may be readily distinguished from malaria by the discovery of the plasmodium in the blood, and also by the greater irregularity of the fever and chills which presents the septic type. In what Osler regards as a very remarkable sub-group of this type, the fever and chills may closely simulate regular attacks of quotidian or tertian ague. In those instances where there has been a previously well-marked malarial infection, the differential diagnosis would become additionally difficult. Again, and despite the affirmation of distinguished observers to the contrary, I have met with undoubted cases of malaria, as I believe, in which no malarial organisms have ever been found, and despite careful and repeated microscopic examinations of the blood by skilled observers.

* British Medical Journal, June 22, 1899.

† Lancet, March 22, 1902.

‡ Thompson. Practical Medicine, second ed., p. 319.

Occasionally chronic endocarditis, accompanied by a fever resembling that of typhoid or remittent fever, may lead to confusion in diagnosis. In these instances, however, embolic phenomena, septic or other, are not found. Moreover, these cases are often prolonged for several months, as in one of Bristow's, cited by Osler. In those cases accompanied with irregular fever, embolic phenomena and physical evidences of recent endocarditis with cardiac distress, and which run an acute course, it is sometimes most difficult to know whether ulcerative endocarditis is present or not. If the case goes rapidly to a fatal termination, as it often does, and we obtain an autopsy, of course the nature of the case can be positively decided. If, on the other hand, the fever, restlessness, cardiac distress, and local signs of heart lesions wholly disappear, and the patient recovers entirely, as in certain recorded instances of gonorrhœal endocarditis (Thayer and Lazear), we may still retain, perhaps, reasonable doubt as to our diagnosis.

The instances which are reported to recover are the less acute forms, and have usually been grafted more than once upon old sclerotic changes of the cardiac valves and orifices. In this category I should be inclined to put some of the gonorrhœal cases. These, however, as we know, are diagnosed at times more by cardiac changes than by septic symptoms.* The mechanical factor in the development of ulcerative endocarditis is not an essential one, inasmuch as the fresh endocarditis does not always arise at the site of the old endocarditis if the latter is present.† The distinction Lenhartz makes between chronic septic endocarditis and malignant rheumatic endocarditis, based on the presence in the former of micro-organisms commonly producing sepsis, is called in question by Litten on the ground of variability of bacteriological conditions, and he states that no distinction can be made on this basis. Stengel finds both classifications unsatisfactory.‡

In these instances much importance should be attached to the supposed etiological factor. If it be of the nature of articular rheumatism, chorea, or scarlatina, we would infer that we had to do with an endocarditis of benign type; if, on the other hand, we find in the antecedents some pus infection or focus of suppuration, puerperal processes, bone-disease, etc., we are prone to believe that ulcerative endocarditis has developed. Again, the febrile movement may be wholly absent, or else pursue a very mild and regular course. In the latter case it is probably due either to the acute endocarditis of simple type, or to the rheumatic cause. When either one gradually subsides the fever also disappears.

With the greatest possible care, however, on the part of the attending physician, the diagnosis of ulcerative endocarditis may be mistaken or overlooked, so frequently do the symptoms vary.§

* Allbutt, p. 882.
† Lenhartz. Gould's Year Book, 1903, p. 182.
‡ Loc. cit.
§ Thompson, p. 319.

Again, as I have pointed out already, there may be a complete absence of recognizable cardiac signs locally. In the acute classes resembling cerebrospinal fever, blood cultures do not help us very much to make an accurate differential diagnosis. If the spinal disease be of tuberculous nature, puncture of the spinal membranes and withdrawal of fluid may be of very great value in revealing the presence of tubercle bacilli. In the non-tuberculous variety, whether it has become suppurative or not, we may find the same organism that is discovered in ulcerative endocarditis, and of course our doubts are in that case not solved by this method of exploration.

The course of ulcerative endocarditis may be very brief. Indeed, it may be a very acute disease, last only a few days, and then terminate fatally. Such are the extreme and relatively rare instances. The more frequent ones are those where the disease has lasted several weeks. Its progress onward and downward may be continuous. On the other hand there may be periods of relative improvement followed by renewed exacerbations. The patients seem to improve for a time and subsequently relapse and return to the hospital in a worse condition. (Glynn.) When death actually occurs it is occasioned by the progress of the heart disease, which finally causes pronounced asthenia. Or again it is the prolonged general sepsis which apparently occasions the fatal outcome. There may be complicating pulmonary œdema or pneumonia, and in this way death occurs more rapidly. Sometimes it would appear that the term of life is closed essentially by reason of emboli in different organs—kidney, spleen, or brain.

An interesting case is reported by Babcock (p. 173 *et seq.*) following an attack of tonsillitis which after five months' duration terminated fatally. In this case, although clearly a septic one from the beginning, the pulse persisted at about the same rate (105), and there was a fairly continuous temperature with slight changes. There was present marked bulbous enlargement of the terminal phalanges of the fingers due to capillary dilatation. Unfortunately in Babcock's case there was no autopsy. Credé's ointment and antistreptococcic serum were employed, with the results perhaps of increasing strength for a while, and occasioning a slight reduction of temperature. The occurrence of emboli always renders the prognosis more serious. In addition to the mere mechanical results of these emboli in the different viscera we observe their septic consequences, which contribute to the speedy, fatal termination. Thus we find single or multiple septic abscesses in the spleen, liver, kidneys, and, indeed, throughout the body, and these are the evidences of general infection of the economy. Of course, death is the inevitable result, almost, of such a condition.

In general the treatment of ulcerative endocarditis is that of acute benign endocarditis with even greater precautions exercised about preserving the strength of the heart, noting that independently of

the specially destructive tendencies of the disease to the cardiac valves and walls and the formation of abscesses locally in its structure the heart muscle is more likely to suffer from the effects of the toxæmia itself than in the relatively benign form of disease. The treatment may be regarded therefore as essentially symptomatic.

To combat general sepsis we should rely upon large and repeated doses of alcohol in the most palatable and useful form—*i. e.*, the best old brandy—alternating it with best champagne now and then for a day or two. The employment of alcohol in septic disease and in sufficient quantity is still heartily endorsed by many eminent clinicians and despite many and strong arguments made use of by its adversaries. Carbonate of ammonia is also possibly a useful adjunct to alcohol for a little while, in view of the thrombotic findings upon the cardiac valves which some autopsies reveal and by reason of the proofs we seem to have, clinically, of its action in lessening somewhat the tendency to such deposits or formations. The late Dr. Benjamin Ward Richardson insists forcibly upon this view as regards certain infectious diseases, notably diphtheria, and I have always believed with much reason. I am satisfied, however, that carbonate of ammonia is far more depressing even than alcohol if too long continued, and particularly in large, frequently repeated doses such as are so often insisted upon in clinical text-books of practice of medicine.

To abate or lessen the chills and the fever quinine is used by some with the idea that it will do so if given in doses of 5 to 10 grains three or more times daily. With our improved knowledge of the etiology and pathology of the disease such a view seems scarcely warranted. And when we think of the cardiac depression which may follow such doses, demonstrated many years ago by Binz, I find no adequate reasons for the use of the drug after this manner. The treatment of disease then, according to many, is practically that of septicæmia (Osler), and except the measures which we should rationally employ in all forms of endocarditis even the mildest.

Are there therefore no known measures which have any curative influence upon the march and termination of the disease itself? Dreschfeld speaks of having been useful by means of a combination of quinine and arsenic in 3 cases, 2 of which he reports.[34] In neither case, however, did recovery take place. Perhaps the prognosis of ulcerative endocarditis may become more hopeful with our improved forms of treatment; more so even than that of the cases of endocarditis which are regarded as relatively and less immediately dangerous.

With the progress of serotherapy and of intravenous medication this statement has become especially true during the past year. This progress is due to researches of pathologists who, like Poynton and Paine, have pointed out the parasitic nature of the disease.

Besides, several histories have been reported pointing to the favorable outcome of the disease through medication. Occasionally recovery may be expected. Clinical reports bear evidence of this, and besides it is more than justified by the results from autopsies.

The treatment of the disease has now definitely in view the killing of the germs. Two methods of medication have been tried —*i. e.*, the sera and the mineral germicides. They may be administered either internally by mouth or rectum, subcutaneously or intravenously. Later all three methods may be combined at the same time to hasten the cure.

As to the relative value of these remedies it is impossible to state at present. But each day seems to show how important has become the interactions between living and inorganic matter. In this line notably are the effects of radium on the tissues. The promulgation of the catalytic action of sera and albuminized metals is also related to our ignorance, but presuming this theory to be correct it would prove how useful the direct application of remedies may be to the cure of disease. An effort has been made to introduce antiseptic remedies in sufficient quantity into the system to exert at least a modifying influence upon the sepsis. (Babcock.) Among these the sulphocarbolate of soda in one-half drachm doses has been used by Sansom, and with such good effect that one patient was enabled to leave the hospital and remain away ten months before a fresh attack occurred. To the latter, however, she succumbed, and the autopsy justified the accuracy of the diagnosis by revealing cardiac valves permeated with micrococci.

Of course if antiseptic medication is to be of real service it must be employed in sufficient amount to affect the system thoroughly, and be continued for a considerable period. And here resides the danger with which we are all familiar, to-day more than ever, that in our efforts to destroy or neutralize micro-organisms and their toxins so pernicious to the economy, we may occasion great harm to the composition of the blood which would more than counterbalance any beneficial results from the use of antiseptic medication. This is especially true if we employ the hypodermic method. In illustration I would refer to the brilliant work of Barrows in the treatment of puerperal septicæmia, who at first seemed to have achieved a very remarkable triumph.

According to the latest laboratory experiments of J. M. Fortescue Brickdale,[35] injection of antiseptics produce no favorable results. This experience is corroborated by W. H. Park and W. A. Payne,[36] who state that in their judgment the use of plain salt and water intravenously will be found equally useful and less dangerous than diluted formalin injections.

On the other hand the use, clinically, of intravenous injections of antiseptics by Netter,[37] Maguire, Landerer, and Ewart, has been at times distinctly favorable. Further, Klotz narrates a case

resulting successfully, in which colloidal silver was used hypodermically. After two injections there were rigors and no improvement; but after the third there was rapid decrease of fever and ultimate recovery.[38]

As Ewart remarks, forcibly, too rigid adherence should not be directed toward mere "germicidal potency" as a test for practical utility. It may be that intravascular antisepsis will prove delusory, but over and beyond is the great subject of intravenous medication which must remain as a very valuable aid to our methods of treatment. Inasmuch as the action of the antiseptic injections is not bactericidal, some other explanation must be given of their power for good. According to Netter this resides in a catalytic action much resembling the action of ferments, and depends upon a mysterious power of matter. In the discussion of Dr. Barrows' paper the majority seem to preserve an open mind as to the desirability of the treatment in any extensive way.[39]

O'Brien[40] has pointed out some of the dangers resulting from intravenous injections—*i. e.*, rigors, collapse, and respiratory embarrassment. In one case sudden death followed. As there was no autopsy a definite explanation could not be given. It is important to note that those who make use of these injections should be prepared to deal with sudden emergencies which may arise.

No doubt there is some comfort to be taken, as Babcock would have us believe, apparently, from the neutralization of the toxins found in the intestinal tract during the course of ulcerative endocarditis, and which doubtless, unless properly neutralized, tend to aggravate the original disease and prevent recovery. Among these so-called antiseptics used to modify favorably autointoxications from the intestinal tract, there are only a few in which I have at present even limited confidence. The best and least harmful which I have tried are small, repeated doses of beechwood creosote, the salts of bismuth, and wood charcoal. In a paper read before the New York Clinical Society about two years ago I directed attention in this connection to these drugs, and spoke favorably of their use as compared to others I had tried.

Up to the time of writing a certain number of cases have been treated by the antistreptococcic serum, and with more or less success. There is a certain degree of reason in the use of this serum, because it appears to be useful in other septic cases—notably puerperal septicæmia. It is also reasonable to employ it because streptococci are undoubtedly among the organisms which appear frequently infiltrated, as it were, in the cardiac valves at the autopsy of these cases. The serum itself, properly employed, does not cause injury to the patient, and again we find in the antitoxin treatment of diphtheria an analogy which makes us somewhat hopeful of this other new treatment. The outlook seems to be, therefore, that pathological sera will probably be more and more

used. Antitoxins and immunizing sera have, indeed, more than one action, and, it has been demonstrated, may be useful in distinct diseases. The explanation of their effects may reside in a catalytic action not dissimilar to that of the albuminates of the metals. The intravenous route is the one now preferable for serotherapy, especially in the severer cases, and when subcutaneous injections have proved ineffective. To the former injections, despite disadvantages and dangers, we should recur hopefully.

Sir Douglas Powell reports three successful cases from the use of antistreptococcic serum, and emphasizes the fact that if it were employed earlier in the disease, and before a general dissemination of it in different organs had taken place, our results would be better. He also considers that in its use we must not expect benefit where organisms of another order, like pneumococci or gonococci, are present, but be hopeful and limit its use to those cases in which streptococci or staphylococci have been causative. If there be anywhere a purulent focus which surgery can reach it must be promptly dealt with and suppressed if possible. Otherwise we should expect continual accessions from this source of the toxic organisms whose influence we wish to combat. Hence, the employment of the antistreptococcic serum must remain useless. On the other hand, if the supply of toxic-bearing bacteria is stopped, and even though many of those already in the blood may be other than streptococci, this serum may prove very beneficial.

To obtain our best, most hopeful results treatment should be begun at an early date, or so soon as the diagnosis approaches a high degree of probability. There are, moreover, evident grades in the malignancy of different cases of ulcerative endocarditis, and it is impossible at first to pronounce as to the precise future course of a given case of the disease. The reported cases of improvement and recovery under more than one sort of treatment makes this fact very clear. Again, we should be encouraged from this standpoint to begin early treatment with the serum. It is always judicious and advisable also, to take blood in a doubtful case for the purpose of culture inoculation and other experiment, even though no profitable determination can always be made so as to fix, if possible, the cause of the disease. (Gibson, quoted by Babcock.) Great care must be taken that the blood obtained for bacteriological examination should not be contaminated. The staphylococcus albus, if found, is due to contamination, and is not the specific cause of the disease. The micro-organism which is most frequently found by cultivating the blood is the micrococcus pyogenes. It has been obtained in many cases of ulcerative endocarditis. If a patient with some valvular disease has irregular temperature, is anæmic, and streptococci are obtained from cultivation of the blood, a diagnosis of ulcerative endocarditis should be made, and the indication is to inject antistreptococcic serum. Blood examination

should not be considered infallible as an aid to diagnosis and prognosis. As Bryant[41] writes in corroboration of Ewing's statement: "The examination having been performed, its results are to be interpreted only in the light of the fullest possible clinical information."

It would appear that ulcerative endocarditis of pneumococcic origin offers little hope for any beneficial result from this treatment. Let us hope that the day is not far distant when a suitable serum will be available for every kind of septic poisoning, no matter what the precise efficient bacterial cause may be. The modern researches of the Klemperer brothers and others give us renewed trust that our wishes may soon be realized. (Babcock.) From 3 cases reported by Babcock he is evidently disposed to make use of the antistreptococcic serum in any future cases he may see, even though the diagnosis may be somewhat doubtful, and provided other treatment has been used in vain. He remarks with justifiable emphasis: "Such cases are so desperate and the prospect of recovery so slight that I believe one is justified in resorting to whatever affords even a chance of benefit; and if an old preparation is employed there is not much danger of producing erythema or articular inflammation, and the remedy cannot prove more harmful than the disease itself, unchecked."* Successful results in the use of antistreptococcic serum in the treatment of ulcerative endocarditis have been reported by Sainsbury and by Pearce,[42] another also by Clarke.[43] The following case reported by Bryant[44] appears to me very convincing: "A boy, aged fifteen years, was admitted to the hospital suffering from mitral disease. He had had several attacks of rheumatism. His temperature was varied and running an irregular course, ranging between 98° and 101.5° F. When he first came under my care he had been in the hospital for nearly two months, and during the whole of the time his temperature had been raised and he had not had any manifestations of rheumatism or of tonsillitis. A bacteriological examination of the blood showed the presence of streptococci in pure culture. A few days afterward the temperature dropped to normal and remained normal. A subsequent bacteriological examination of the blood was negative. I considered this boy was suffering from infective endocarditis, that the acute process had subsided, and the streptococci died out."

In some cases of ulcerative endocarditis treated with antistreptococcic serum, while temporary benefit may result from its use, the result ultimately has been fatal. An instance of this kind is described by H. M. Cooper.† In this, as in other cases, it was thought if the serum treatment had been instituted earlier a succesful result might have been obtained. Per contra, as regards the matter of the innocuousness of these injections, the following cases are interesting and important. B. M. H. Rogers[45] used five injec-

* Loc. cit., p. 797.

† British Medical Journal, May 10, 1902.

tions of 10 c.c. each of antistreptococcic serum in a case of ulcerative endocarditis, in which pure cultures of streptococcus had been obtained from the blood. The injections caused violent pain, were without effect, and death occurred. Post-mortem cultures yielded streptococci. J. H. Abram[46] reports another case treated in a similar manner after streptococci had also been found in the blood. The case was fatal; but it was found after death that the streptococci had disappeared. The serum is believed to have caused this disappearance.

Cyril Ogle[47] indicates the value of antistreptococcic serum in cases in which the symptoms during life, or the post-mortem findings, showed ulcerative endocarditis. Of course, the cases are not favorable ones in view of the constant passage of the blood current over the surface of the affected organ—*i. e.*, the heart. Still, recovery is not incompatible with this grave infection when thus treated. In Dr. Ogle's table the successes amount to 31.5 per cent.; in Sir Douglas Powell's tables, to 25 per cent.[48] On the other hand, Nathan Raw used antistreptococcic serum in 5 cases without any beneficial results. And Glynn reports no information of an encouraging nature from Liverpool hospitals, and without success in 3 of his own cases. I find 1 successful case reported by Moritz,[49] in which antistaphylococcic serum was employed. Six injections of 5 c.c. were sufficient to dissipate the acute symptoms. When they were begun the patient had been ill during two months. In two weeks of treatment the temperature was normal. Six weeks later a heart murmur was present and the pulse was rapid. Still the man remained in good condition.[50] Other methods of treatment have also been followed by reported cures. One by Coleman which followed vaccination. Another from Hepburn in which the treatment was entirely symptomatic. In one instance the aortic murmur disappeared during convalescence. The treatment was by the Brand method and unguentum Credé.[51] Roussell[52] reports three recoveries. Another recovery of gonorrhœal endocarditis is from a paper of Lenhartz.*

The employment of yeast in the treatment of ulcerative endocarditis is referred to by Sir Douglas Powell, and 1 successful case out of 5 is reported by him. In the other case there was no appreciably good result. In one other instance where nuclein was employed there was a decided lowering of temperature. The remedy was employed subcutaneously. If yeast has any remedial value it is probably due to the nuclein or nucleinic acid it contains, as instanced by Vaughn. The latter may be used by mouth, rectum, or hypodermically, according to the strength and kind of preparation made use of. It would seem as though the curative action of the nuclein was essentially due to its power of increasing polynuclear white cells. These, as we know, are frequently more

* Loc. cit.

numerous in ulcerative endocarditis, and the germicidal properties of nuclein are explained by their additionally increased number. Many favorable reports, according to Babcock, have been made about the value of yeast-nuclein in the treatment of divers pus infections. And in view of these statements he was encouraged to give it a trial in a case of acute endocarditis complicating a follicular tonsillitis, possibly of rheumatic origin. During the period the remedy was taken the fever slowly abated. Despite this fact, however, the case terminated fatally. Latterly, Duckworth reports, in the Section of Medicine of the Fourteenth International Medical Congress (Madrid, April 25, 1903), a case of probable ulcerative endocarditis in which a treatment with fresh yeast and antistreptococcic serum hypodermically was employed without appreciable benefit. Subsequently, however, a cure was apparently effected by repeated injections per rectum of a mixed antistreptococcic serum, 10 c.c. being the dose employed.* "This case may be taken," writes Duckworth, "to illustrate the effects of a specially virulent quality or variety of the specific infecting microbe which commonly induces ordinary rheumatic symptoms, and may add support to the view of Poynton and Paine that infective endocarditis may sometimes be a primary affection due to a virulent form of the peccant matter of rheumatism."

If all endocarditis should be properly regarded as infective, it is indicated to find our remedial agent among the class of antiseptic remedies. The most available and least objectionable is the one to make trial of. Amidst the rapidly increasing number of this class of remedies one will be ultimately found that is decidedly curative in many instances. Of course, in making use of the antiseptic remedy so as to influence the entire mass of blood and prevent the infection from being carried to and localized upon the endocardium, we should avoid strictly employing remedies which threaten the general health. At present, moreover, we make use of such remedies mainly in the treatment of the supposed virulent cases, and usually at a later stage of the disease when the outcome is almost surely fatal. In the far larger class of benign cases of endocarditis, and hence the more important ones, their progress is often not stayed by this or any other careful treatment soon enough. The result is they continue their onward insidious and disastrous march. If these cases were treated in the beginning by judiciously selected antiseptic remedies, it is to be hoped that eventually we should have fewer cases of both sorts, and mainly, I believe with Ewart,[53] of the ulcerative forms. Further, we should not be obliged to admit, as it seems to me, with the writer of the latest and most valuable treatise on diseases of the heart, "that the most the physician

* Lancet, May 2, 1903, pp. 1268, 1269; and Boston Medical and Surgical Journal, August 29, 1903, p. 238.

† British Medical Journal, May 23, 1903, p. 1195.

can do in the treatment of acute endocarditis is to aid nature by helping to maintain the vital powers that lie in nature's way."[54] Let us remember that recovery in an apparently desperate case is possible, and the future may bring improved methods both of serum and antiseptic treatment.

It may be well to add that the latest experiments upon animals seems to prove that the Aronson antistreptococcic serum is superior to the others, notably those of Marmorek and of Tavel. It is apparent, also, that to obtain the best curative effects the serum should be given intravenously. Also, treatment according to this method should be continued well into the period of convalescence, inasmuch as death occurs sometimes when all danger seems to have passed.

Finally, I would again insist upon the primary importance in all cases of beginning the use of the serum at an earlier date than hitherto has usually been done. Sometimes, not to say frequently, it has been employed when all curative methods must prove futile, as the economy is unable to respond favorably to that as to all other medication. Moreover, whenever the infection has lasted more than a very brief period much larger doses of serum are rendered necessary to produce similar curative effects. I shall not attempt to explain how the serum acts. Nor, indeed, is it positively known. Certainly it has no appreciable effect upon the growth of cocci in the culture tube, and it appears in final analysis merely, so far as our knowledge now extends, to diminish *virulence*, "for cocci which have been left for some time under the influence of the serum will no longer bring about hæmolysis."[55] The latest paper on the use of "antistreptococcic serum in the treatment of inflammatory rheumatism and other diseases" is to my mind very encouraging. It shows conclusively it is most efficient when given *early* in infectious disease; also, that it is useful in *diplococcic* infection. In Dr. G. H. Sherman's[56] cases "none of the patients developed heart complications, and complete recovery took place in a comparatively short time." This statement contradicts that of Osler—*i. e.*, "We know no measures by which in rheumatism the onset of endocarditis can be prevented."*

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1. Medical News, March 21, 1885.
2. London Lancet, March 25, and April 2 and 9, 1898.
3. Loc. cit., April, 1903, p. 1153.
4. Practice of Medicine, 4th ed., p. 699.
5. Loc. cit., p. 700.
6. Progressive Medicine, September 1903, p. 79.
7. Practice of Medicine, 6th ed., p. 595.
8. C. S. Bull. Medical Record, December 20, 1902.
9. Johns Hopkins Hospital Bulletin, October, 1902.
10. Progressive Medicine; also Deut. med Woch., May 22 and 29, 1902.

* Vide fifth edition, 1903, p. 705.

11. To show the extreme rarity, even with typhoid fever, I would cite Dr. Osler's medical clinic at the Johns Hopkins Hospital, where there never has been a case (written communication from Dr. W. S. Thayer, December 10, 1903). Very probable cases, in view of the symptoms during life, are occasionally met with. Even in fatal cases with characteristic symptoms, where no autopsy is obtained, doubt as to diagnosis may be urged, although in one of Dr. Thayer's cases such doubt would hardly be justified.

12. Wells says this complication is very frequent.

13. THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, January, 1901, p. 58.

14. Austen. Johns Hopkins Bulletin, 1899, p. 104.

15. American Medicine, October 17, 1903, p. 627.

16. Journal of Experimental Medicine, 1899, p. 521.

17. Journal of the American Medical Association, August 19, 1900.

18. Progressive Medicine, September, 1903.

19. Gould. American Year Book of Medicine and Surgery, 1903, p. 752.

20. Progressive Medicine, September, 1902, p. 128.

21. Allbutt's System of Medicine, vol. vi. p. 876.

22. Practice of Medicine, 4th ed., p. 701.

23. The vegetations themselves, although unrecognized during life, may have been present for a long while, as shown by autopsy.

24. Dessy. Boston Medical and Surgical Journal, September 1, 1898.

25. Journal of Experimental Medicine, January, 1899.

26. Rev. mens. des mal. de l'enfance, December, 1898.

27. Diseases of Infancy and Childhood. 2d ed. p. 622.

28. The exceptions to this rule would appear to be cases of gonorrhœal origin where the right heart is frequently involved (Thayer and Lazear).

29. Semaine méd., January 21, 1900.

30. Practitioner, November, 1898.

31. Medical News, July 23, 1898.

32. The duration in the fatal cases is only a few days or weeks, but in those that recover it is usually much more prolonged.

33. According to MacFarland there was in 4000 cases only 4 per cent. of error (Babcock, p. 182). If after sixth day of illness test is negative, typhoid fever may be properly excluded (Allbutt, foot-note).

34. Allbutt's System of Medicine, vol. vi. p. 884.

35. Lancet, January 10, 1903.

36. Medical News, April 4, 1903.

37. Bull. et mém. de la Soc. des hôp. de Paris, December 18, 1902, et seq.

38. Progressive Medicine, September, 1903, p. 81.

39. New York Medical Journal, January 31, 1903.

40. Lancet, October 11, 1902.

41. Ibid., February 7, 1903, p. 364.

42. Allbutt's System of Medicine. Loc. cit., p. 885.

43. Lancet, July 21, 1900.

44. Ibid., February 7, 1903, p. 364.

45. Ibid., June 10, 1899.

46. Ibid., February 25, 1899.

47. Ibid., March 14, 1903.

48. Ibid., April 25, 1903, p. 1153.

49. Serum therapie bei Endocarditis Maligna, St. Petersburger medicinische Wochenschrift, 1898.

50. In Moritz's case the diagnosis of the organism present had not been confirmed previously by a blood examination, although the evidence of implication of the valves seems to have been certain (Lancet, March 14, 1903, p. 723).

51. Philadelphia Medical Journal, January 12, 1901.

52. Ibid., February 23, 1901.

53. Progressive Medicine, September, 1902, p. 112.

54. Babcock, p. 198.

55. Medical News, September 5, 1903, p. 462.

56. American Medicine, October 17, 1903, p. 633.

NOTE.—Owing to the length of this paper, I am obliged to omit the histories of my cases.

In Bulletin of the Ayer Clinical Laboratory of the Pennsylvania Hospital, October, 1903, a unique case is reported of ulcerative endocarditis caused by Weichselbaum's meningococcus.

REMARKS ON GASTROSUCCORRHŒA AND TETANIC ATTACKS OCCURRING WITH CHRONIC ULCER OF THE STOMACH.[1]

By J. Kaufmann, M.D.,
of New York.

Ever since analyses of gastric contents have been made in order to study the function of the stomach and its disturbances mistakes have been made chiefly in two directions: certain functional disturbances which are really only symptoms have been stamped as diseases, and in explaining certain conditions too much stress has been laid upon secretory disturbances, the importance of motor disorders being underestimated. This applies also to the picture described as gastrosuccorrhœa. Although much has been written about this symptom-complex, there is still a great deal of confusion in regard to its correct interpretation, and it is therefore justifiable to consider once more whether this picture ought to be taken as an independent disease.

Reichmann was the first to apply the name "gastrosuccorrhœa" to a set of symptoms which are chiefly characterized by the presence in the fasting stomach of a fluid possessing all the chemical and physiological properties of gastric juice. The patients, who are generally emaciated, complain of pyrosis, eructation, and vomiting of highly acid matter, and suffer a great deal from gastric pains coming on after meals and during the night. Examinations of the stomach contents after test meals show hyperacidity and impaired digestion of starches. In the urine there is often a diminution, and sometimes even a total absence, of chlorides. In Reichmann's opinion the characteristic feature of this condition is the continual flow of gastric juice, not only after meals and during the process of digestion, but also during the intervals when the stomach of a normal individual should be empty.

Reichmann's publication aroused an extensive and lively discussion of the questions: Is gastrosuccorrhœa, as its name indicates, really a primary secretory disturbance, or is the accumulation of secretion in the fasting stomach the result of a motor insufficiency? Is gastrosuccorrhœa a disease *per se*, or is it merely a peculiar combination of symptoms which accompany other already well-known pathological conditions? A consensus of opinion on these questions has not as yet been reached.

There are two varieties of gastrosuccorrhœa—the periodic and the chronic. In the *periodic form* we have to deal with attacks of vomiting of gastric juice, coming on spasmodically and lasting from

[1] Read before the German Medical Society of the City of New York, April 8, 1902.

a few hours to several days. The condition has been attributed to a morbid overactivity of the secretory nerves of the stomach, which is regarded as a neurosis by itself, as a symptom accompanying hysteria or neurasthenia, or as a symptom occurring in the form of gastric crises in tabes and other spinal diseases. The remaining symptoms occurring with such attacks, pyrosis, headache, gastric pains, and vomiting, are classed as secondary manifestations. The same attacks have, however, been described by a number of other writers under different titles, the name depending upon the symptom regarded as being the most important. Thus, Leyden refers to them as "periodic vomiting;" Struebing classes them with disorders which he designates as "angioneurotic œdema;" Rossbach, who considers the increased secretion of hydrochloric acid as the chief factor in the condition, calls them "gastroxynsis." They are also found in descriptions of nervous diseases. Möbius, for example, associates them with migraine. I shall not further discuss this group of cases of periodic gastrosuccorrhœa, the pathogenesis of which is still very vague. The secretion of large quantities of gastric juice accumulating in the stomach independently of the ingestion of food may play an important role. However, all that has thus far been taught about the relation of the various symptoms to one another, and especially in regard to the point whether this increased secretion of gastric juice is the primary or only a secondary factor in the attacks, is still altogether hypothetical.

In *chronic gastrosuccorrhœa* the conditions are entirely different, since it is not of a nervous character, but is dependent upon anatomical changes of the stomach or duodenum. In these cases it can be demonstrated that the presence of fluid in the fasting stomach invariably means a motor disturbance, and that the view that chronic gastrosuccorrhœa is a disease *per se* is not well supported.

As has already been mentioned, Reichmann's theory was that the characteristic feature of the disease was the presence of gastric juice in the stomach at a time when the organ should be empty. According to his view, this accumulation of gastric juice occurs because the mucosa of the stomach secretes continuously without any apparent irritation, but solely in consequence of the morbid activity of the secretory nerves of the stomach.

Reichmann, however, did not overlook the fact that the presence of gastric juice in the fasting stomach could not be explained simply as a hypersecretion. In some of the cases described by him as much as a litre of fluid rich in hydrochloric acid could be expressed in the morning. In these cases there was undoubtedly an increased secretion, but this is by no means the rule. In a number of other cases the quantity found was decidedly less. The amount of hydrochloric acid contained in the fluid also varies. In cases where only relatively small quantities are found, or where the amount of hydrochloric acid is low, we cannot very well speak of increased secretion,

especially as we do not know the quantity secreted by the normal stomach during a given time. The essential point, therefore, is not that there is an increased secretion, but is rather in the fact that this secretion is found in the stomach at a time when the organ ought to be empty.

The opinion was formerly held that the fasting stomach of a healthy individual was entirely empty. This view has since been somewhat modified, Rosin and Schreiber having reported that in systematically examining a large number of healthy individuals they often found gastric juice in the fasting stomach in varying quantities, sometimes reaching 40 c.c. Martius, Hemmeter, and others have confirmed these statements. The gastric secretion in these cases is explained as being the result of the stimulation caused by swallowed saliva and pharyngeal mucus.

However that may be, quantities of 50 c.cm. and over are surely pathological. Where such quantities are found it is possible that gastric secretion has been increased and kept up beyond the time required for digestion. But the fact that it is found in the fasting stomach can only be explained by the existence of some hindrance to its passage into the intestine. For, if motor function of the organ is normal, there is no reason why such increased secretion should not pass into the intestine just as well as other stomach contents.

The misinterpretation of these conditions was partly due to the singular confusion which followed the discussion of the meaning of gastric dilatation. I shall not enter into the discussion of this subject further than is necessary for understanding its relation to gastrosuccorrhœa. There is no reason for discarding the old, well-defined clinical picture of gastric dilatation. Its characteristic feature is that it is a combination of two conditions which must be distinguished: the enlargement of the organ and the stagnation of stomach contents. Enlargement of the stomach is an anatomical condition. Stagnation of stomach contents represents a functional disturbance—a motor insufficiency. A stomach with normal motor activity, no matter what its size, empties its contents during the night. Where this is not accomplished motor insufficiency is present.

The stagnating material may consist principally of solid food remains mixed with a larger or smaller quantity of fluid, or it may be chiefly fluid containing few or no solid particles. When solid particles are found, all authorities agree on the presence of stagnation. But when only fluid can be expressed from the fasting stomach, as is often the case in gastrosuccorrhœa, some authors maintain that the condition cannot be considered a stagnation, because no solid particles are contained in the fluid. To support this view, it was argued that in some of these cases certain symptoms generally associated with gastric dilatation were absent. It was claimed, for instance, that in cases where no lowering of the greater

curvature could be demonstrated there could be no dilatation of the organ, and therefore no motor insufficiency.

In diagnosing dilatation of the stomach we must separately consider three things: (1) the size of the stomach; (2) its position, and (3) its mechanical ability.

Size and position of the stomach do not necessarily indicate its mechanical ability. A stomach may be very large and its greater curvature may be low, yet it may be motorily sufficient. In such a case we cannot speak of dilatation, but simply of a deeply situated, enlarged stomach—megalogastria. On the other hand, a stomach may be high and its motility be insufficient. This very condition is not infrequently found with gastrosuccorrhœa. We shall see later on that in these cases we have to deal with gastric ulcer. When the ulcer is situated at the lesser curvature and there are adhesions to the surrounding tissues, the stomach remains high, and in case of dilatation extends upward. In these cases I have frequently seen the fundus of a stomach almost reach the axilla in the dorsal position. When the lesser curvature is thus fixed the greater curvature may remain above the umbilical line, even in cases of pronounced dilatation with decided stagnation of the stomach contents. Hence, a high position of the greater curvature cannot be regarded as proving that in a given case no gastric dilatation is present, and, therefore, no motor disturbance.

Just as invalid is the argument that in certain cases of gastrosuccorrhœa no motor insufficiency was present because certain forms of fermentation were absent, particularly the gas fermentation. It is true that whenever there is stagnation in the stomach fermentation sets in. There are, however, various fermentations in the stomach, brought about by different organisms and leading to different fermentation products. The absence of any one form does not indicate that all fermentation is absent. By careful analysis some form of fermentation can always be demonstrated.

As for the statement that a motor insufficiency cannot be present when the stomach contents expressed in the morning do not contain food particles, it must be said that actual findings do not justify this conclusion. Reports of autopsies in such cases, where only fluid could be obtained without food particles, showed pyloric obstruction with ulceration. Also, it must be remembered how difficult it is to empty the stomach entirely when dilatation is present.

We may add that in the majority of cases this fluid actually contains food particles. If we examine the histories of typical cases, as reported by Reichmann and others, we find it especially stated that the fluid expressed from the fasting stomach contained varying amounts of food particles, principally starches, and also sarcinæ, which, beyond doubt, indicate motor insufficiency.

From the foregoing statements, therefore, we see that all argu-

ments brought forward to explain the presence of larger quantities of gastric juice in the fasting stomach merely as a result of secretory disturbance without motor insufficiency are invalid. We must insist that the accumulation of acid fluid in the fasting stomach is always the result of motor insufficiency. This motor insufficiency may be due to atony of the stomach or to organic or spastic stenosis at its outlet.

Let us now consider the question: Is chronic gastrosuccorrhœa a disease *per se?* The fact that the presence of gastric juice in the fasting stomach always means a retention of secretion due to motor insufficiency does away with one argument often put forth in support of the theory that gastrosuccorrhœa is a primary and independent secretory disorder—the argument that the secretion of gastric juice takes place without the influence of direct irritation (stimulation by food), but purely as the result of the pathologically increased activity of the secretory nerves. For even small quantities of food particles are sufficient stimuli for the secretion of gastric juice, particularly when they lie directly on an ulcer, and when nothing but fluid is retained this stagnating fluid acts as an irritant. The more sensitive the mucous membrane the greater the quantity which it will secrete. The constant irritation of this stagnating fermenting fluid must in time increase the irritability of the mucous membrane and lead to anatomical changes.

Examinations of the mucous membranes in these cases, made at first by Korzynski and Jaworski, and later by Hayem, Hemmeter, Strauss and others, show a definite form of gastritis characterized by a destruction of the chief cells, the parietal cells remaining intact. There was often found a proliferation even up to the formation of polypi.

In opposition to the view which considers the gastritis a result of the permanent irritation by the stagnating masses, due to the motor insufficiency, some authors claim that the gastritis is the primary element of the whole process, and assert that the inflammation of the mucosa alone suffices to cause an abnormal irritability and an increased and continuous secretion of gastric juice. Even the development of gastric ulcer is attributed to this gastritis.

Granting that the gastritis plays an important part here, it seems to me that there is no reason for dwelling on the question whether the motor insufficiency or the inflammation of the mucous membrane is the primary disturbance. Both are factors in producing gastrosuccorrhœa; in some of the cases the motor insufficiency being the primary trouble, in others the gastritis.

However gastrosuccorrhœa is brought on, since we have seen that gastric juice in the fasting stomach always means a motor insufficiency, there can be no doubt that the stagnating secretion keeps up and increases the inflammation of the mucous membrane.

It is clear from the above explanation that where motor insuffi-

ciency and increased secretion go together a retention of gastric juice can take place. Such simultaneous occurrence of motor and secretory disturbance is often found during the course of various diseases of the stomach. Thus the presence of the gastric juice in the fasting stomach is a condition frequently observed in gastritis acida with atony, atony with secondary gastritis and hypersecretion, pyloric and duodenal stenosis resulting from adhesions or compressions, etc. It is obvious that in all these diseases gastrosuccorrhœa can only be considered as a symptom.

Some authors apply the term gastrosuccorrhœa to all cases where gastric juice is found in the fasting stomach. Others maintain that we ought to distinguish between the cases where the presence of gastric juice in the fasting stomach is only a symptom, and another well-defined group of cases for which they would reserve the term gastrosuccorrhœa. They claim that the presence of gastric juice in the fasting stomach does not justify a diagnosis of gastrosuccorrhœa unless the completely developed symptom-complex of Reichmann is also present. They regard this symptom-complex (Reichmann's disease) as a sharply defined, typical picture, showing, besides the characteristic presence of hydrochloric acid in the residual fluid, a number of other symptoms—pyrosis, vomiting, loss of flesh, and, most important of all, of severe pains occurring after meals and during the night.

If we now scrutinize this limited group of cases, in which the symptom-complex of Reichmann is fully developed, it must be said that even for this group no proof has yet been given that gastrosuccorrhœa occurs as a disease *per se*. In fact, whenever an operation or an autopsy has afforded an opportunity to gain an anatomical basis it has revealed ulcer or its sequelæ. Thus we see that even in these cases, which apparently are so well defined, gastrosuccorrhœa is only an accompanying symptom of a well-known disease—*i. e.*, gastric ulcer.

As long as we have no proof that gastrosuccorrhœa may occur as an independent disease we shall do well to regard it merely as a symptom. In this smaller group of cases in which the combination of symptoms given by Reichmann is completely developed and where severe gastric pain plays an important role, we shall not err if we regard it in every case as a symptom of gastric ulcer. If we look upon gastrosuccorrhœa in this light as a symptom, it becomes a valuable aid in diagnosing certain cases of gastric ulcer. Whenever we find a patient suffering from gastric pains coming on regularly after meals and especially at night, with or without vomiting, the presence of acid fluid even in small quantities in the fasting stomach indicates ulcer of the stomach. Hemorrhage and perforation, the most characteristic symptoms of ulcer, are observed only in a certain percentage of the cases. In the remaining cases gastric ulcer may present many different clinical forms, among which

Reichmann's symptom-complex stands out as a very characteristic and typical picture.

As a rule, in cases which develop gastrosuccorrhœa the ulcer is situated near the pylorus and causes a mechanical obstruction, generally by spasm of the pylorus. This spasm, which brings on severe pain, usually occurs after the greater part of the stomach contents have passed into the intestines. That frequent spasms do really occur here is proved by the finding of a strongly hypertrophic pyloric ring.

In the treatment of gastrosuccorrhœa it is of great practical importance to have clearly in mind the fact that the motor disturbance plays a more important role than the secretory, and, further, that the well-developed symptom-complex of Reichmann is not a disease *per se*, but a symptom of gastric ulcer. We accordingly treat the condition by freeing the stomach from its stagnating contents, also using methods usually resorted to in gastric ulcer. Cures by such treatment have often been reported, and my own experience is corroborative.

In cases which do not yield to methodical internal treatment for ulcer one should not hesitate to do away by operative interference with the hindrance at the pylorus, which is really the principal cause for the whole trouble. We are more apt to come to this decision when we are certain that we have to deal with ulcer and pyloric obstruction than when we regard gastrosuccorrhœa as a disease *per se*, caused simply by an increased irritation of the mucous membrane. In the literature there are descriptions and post-mortem reports of fatal cases of gastrosuccorrhœa which give one the impression that had the cases been diagnosed as ulcer with pyloric stenosis, and promptly operated upon, the patient could have been saved. In all the cases with Reichmann's symptom-complex which have come under my own observation and which were operated upon, the diagnosis of ulcer was confirmed.

I wish to describe one case in detail because it presents another interesting condition with which gastrosuccorrhœa stands in intimate relation, namely, tetanic attacks.

History. In May, 1898, the patient, aged forty-four years, stated that for the past two years he had suffered with heartburn and gastric pain of a dull and at times even intense character, occurring several hours after eating, but particularly at night. In the morning, before eating, he was troubled with a gnawing sensation in the stomach and gaseous distention; no vomiting; bowels regular. The trouble had been regarded as nervous dyspepsia and treated as such.

The patient was tall, thin, had a long thorax with healthy thoracic viscera, a flat abdomen and normal outlines for liver and stomach, the pyloric end being painful to pressure. Urine now and later

throughout the whole course of the disease free from albumin and sugar and contained a moderate amount of indican.

Examination after test meal (tea and toast) showed moderate hyperacidity with impaired amylolysis. Alkalies and a suitable diet relieved the subjective symptoms for a few months, during which time patient gained six pounds. In the fall the symptoms returned with increased intensity, particularly the pains during the night.

Stomach analysis of November 19th showed strong hyperacidity. As ulcer had been suspected from the beginning, a treatment for ulcer was suggested, but again refused, as formerly. The patient did not place himself under treatment until the end of January, 1899, when the pain became so intense that it robbed him of sleep.

The first lavage (February 16th) showed a black fluid without food particles in the fasting stomach, so that there could be no more doubt as to the presence of an ulcer. From then on rest in bed. For four days nourishment exclusively by rectum—then in the morning Carlsbader Mühlbrunnen and, besides the enemata, milk per os, at first in small quantities, gradually increasing.

Since three weeks of this treatment gave but little relief from pain, and alkalies, bismuth, belladonna, codeine only relieved the patient temporarily, lavage was taken up and after the washing bismuth was introduced. The fasting stomach nearly always contained from 50 cm. to 100 cm., and occasionally more, of a strongly acid fluid, mostly stained with blood and often mixed with some remnants of food of the previous days.

The bismuth treatment alleviated the pain but little. Irrigations with silver nitrate (1:1000), which were begun two weeks later, also produced little effect. Changes in the milk diet (cooking with fine flour, peptonizing, sour milk) and a trial of thick gruels and soups gave no better results. On the contrary, during the second half of March the pain increased in intensity and duration. Since the rigidly applied internal treatment failed absolutely, operation was advised on March 24th, but had to be postponed several days for ulterior reasons.

During this time there was a decided change for the worse. Until then the quantity of fluid found in the fasting stomach had been relatively small, even when larger quantities had been ingested. During the middle of March, with the increase of pain, the amount of stagnating fluid became greater. From the 24th to the 29th signs of complete pyloric obstruction set in, with almost continual excruciating pains. Although smaller quantities of food were taken the amount drawn from the stomach increased; rapid diminution of urinary secretion, which so far had been plentiful; skin dry; emaciation more marked. Now, for the first time, a hard, painful resistance could be felt in the pyloric region.

March 25th. But little nourishment was taken; during the night, after most violent pains, for the first time there was vomiting of

blood-stained fluid. In spite of the large quantity of the vomitus, and although nothing had been taken afterward, 750 cm. of fluid were withdrawn from the stomach in the morning of March 26th. During this day the patient took only 180 c.c. each of milk and Vichy. Yet in the evening, when the continual severe pain made it necessary to again introduce the stomach-tube, as much as 1100 c.c. of blood-stained fluid was obtained—that is, three times the quantity taken during the whole day. Upon standing a thin, reddish-film formed on the surface of this fluid, the remainder consisting of clear, light green liquid, with a very high percentage of hydrochloric acid.

During this last introduction of the stomach-tube violent vomiting set in, and with it appeared tonic spasms of arms and legs, both being stiffly extended, the fingers in obstetrician's position. The spasm lasted several minutes. Feeling of numbness in the extremities. Trousseau's phenomenon negative.

27th. A total of 600 c.c. of milk was ingested. In the evening a litre of sanguineous fluid of intensely acid reaction was removed. During the withdrawal of this fluid through the tube (this time without vomiting) both upper extremities became tonically extended, the fingers of the left hand were extended, those of the right in the position of a penman. The spasm relaxed slowly several minutes after the washing was finished. Lower extremities not affected this time. Trousseau's phenomenon negative.

28th. Condition improved. Pain diminished. Larger quantities of milk taken, and it passed into the intestine. Urinary secretion again reached 1000 c.c.

29th. Patient was taken to Dr. Lange's clinic. Lavage of the stomach at 11 A.M. One hour later sudden violent pain in the gastric region and symptoms of collapse. Pulse small; face pale; syncope; abdomen drawn in; liver dulness normal. All the abdominal muscles rigid as boards, several fibres standing out as sharp ridges above the level of the skin. Less pronounced cramps in the muscles of the trunk and extremities. The extremely painful tetanic contraction of all the abdominal muscles remained unchanged for hours, despite the injection of morphine and a mild anæsthesia from ether and chloroform.

Four hours after the perforation laparotomy was performed. The anterior wall of the stomach showed a flat, almost circular swelling, about 5 cm. in diameter, its firm edges extending downward to the greater curvature, and its right limit being still several centimetres removed from the pylorus. The serous covering of the swelling lay free in the peritoneal cavity, only its median edge being adherent to the omentum. Exactly in the centre of the swelling was a sharp-edged opening of the size of a pin-head; there was some turbid fluid in the neighborhood of the perforation.

A segment as broad as a hand was resected, which included the

antrum pylori and the pylorus; suture of the stomach end; duodenal end joined to the posterior wall of the stomach by a Murphy button. The resected piece, cut open along the lesser curvature, showed on its inner surface an ulcer as large as a fifty-cent piece, with an uneven terraced surface, a very thin floor, and firm, undermined, wavy edges. Cut surface through this edge showed firm, white lines. Microscopically, adenocarcinoma. The pylorus thickened but patent. Microscopic examination of the pylorus showed greatly hypertrophied muscles, but no signs of carcinoma.

The healing of the wound progressed smoothly. Nourishment at first per rectum. Upon giving food by mouth recurrence of pyrosis and pain in the stomach; perhaps this can be partly accounted for by the retention of the Murphy button. These complaints, which were somewhat relieved by alkalies and washing of the stomach, manifested themselves after each meal, no matter what kind of food had been taken; and they continued to disturb the patient in the most annoying manner during the following months almost up to the time of his death.

An examination after test breakfast on May 25th again revealed considerably increased gastric secretion. Repeated examinations made after this date showed the continuance of hyperacidity for a remarkably long period, in spite of the development of metastatic tumors.

During the first few months following the operation the patient recuperated and gained in weight. In September the pyrosis and pain became worse again; all attempts to influence the secretion medicinally by means of alkalies, bismuth, atropine, etc., were fruitless.

At the end of September signs of decided stagnation set in, with intense pain and vomiting, so that stomach washings were again resorted to and continued until death, on November 19th, at first once a day, then with increasing stenosis, both in the morning and at night. Upon resuming the lavage the tendency to tetanic spasms recurred, and they were more or less pronounced until within a few weeks before death. They generally manifested themselves in extension of the fingers and hands, more rarely of the arms and legs, and lasted at times only half a minute, but occasionally several minutes.

As early as the end of May—two months after the operation—a distinct resistance could be felt at the umbilicus, and four weeks later hard masses were palpable in the abdomen to the right of and below the scar. They grew to be larger than a fist, pushing the abdominal wall forward. On September 23d, when these tumors had already gained very considerable size, the stomach contents still showed a very high percentage of hydrochloric acid. From the middle of October, however, the quantity of this acid decreased rapidly, and lactic acid appeared. From the end of October the large, fermenting residual masses smelt foul, almost fecal.

EPITOME. We have to deal here with a case of gastric ulcer which became carcinomatous in a comparatively short time. To be sure, the duration of the ulcer cannot be accurately determined. The symptoms of which the patient complained for several years had been regarded by competent physicians as manifestations of nervous dyspepsia. Cases of gastric ulcer which are diagnosed as nervous dyspepsia are by no means rare, and here we have another instance of it. But here, as in many other cases, it was the persistency of the pain that aroused the suspicion of the ulcer, which suspicion proved perfectly justifiable when lavage of the stomach showed sanguineous contents. Yet this ulcer had certainly existed some time before this proof was obtained, and had already involved the deeper layers of the stomach, for the operation, performed only six weeks later, showed an ulcer involving the whole thickness of the gastric wall, with firm, undermined edges, which had already undergone carcinomatous degeneration.

On looking back over the history of the case, therefore, we will not err if we presume that all the symptoms which the patient showed during the last three years of his life, including those taken for nervous dyspepsia, were caused by this ulcer, since during all that time the pains varied only in intensity, their character remaining the same throughout.

At the operation we found that the ulcer was situated several centimetres from the pylorus; the pylorus itself was patent and free from carcinoma, but showed greatly hypertrophied muscles.

This hypertrophy can be explained as a result of the frequent spasms which evidenced themselves clinically by the severe pains. The spasms occurred particularly during the night. For how long a period they had caused stagnation of the gastric juice, with or without food remains, cannot be determined, since for a long time the patient refused lavage. When we commenced to evacuate the stomach regularly in the morning the patient had already been in bed for weeks, living exclusively on a milk diet. In spite of these favorable circumstances, there were nearly always found in the fasting stomach quantities varying from 50 c.c. to 100 c.c. of very acid fluid, often containing food particles. Later the residual fluid became greater when the increase of pains in duration and intensity indicated longer spasms, and shortly before the perforation took place there set in under almost unceasing pains long-continued spasms, which caused extended periods of pyloric obstruction. It was this protracted period of pylorospasm which brought about the retention of the large quantities of excessively secreted gastric juice.

When cases like the one just described are considered without prejudice there can be no doubt that the main cause for the accumulation of such large quantities of gastric juice is given in the spastic stenosis which prevents the passage of the secretion into the bowels.

The more severe and the longer the duration of the spasm the larger the amount of fluid.

Tetanic Attacks. When the spastic stenosis in our case became more pronounced and large quantities of stagnating gastric juice were vomited or removed through the tube, tetanic attacks set in. These recurred in a milder form several months after the operation, when the increasing stenosis at the outlet of the stomach again required lavage. We find the same conditions in nearly all the cases of gastric ulcer with pyloric stenosis in which tetany develops: there is always the evacuation of large quantities of gastric juice, either by vomiting or through the tube. This points to the possibility that the withdrawal of such large quantities of chlorine which are not replaced causes certain changes in the system predisposing to the occurrence of tetanic attacks. We shall discuss this point later on.

In our case, as in many others, it was the lavage which furnished the direct irritation which reflexly brought on the spasm. Remarkable, however, is the severe and long-continued tetanic contraction of the abdominal muscles in connection with the perforation. Contraction of the abdominal muscles is, indeed, a well-known symptom of perforation into the abdominal cavity. In this case, however, where a strong tendency to spasm, perhaps due to the deficiency in chlorine, already existed, the perforation was the exciting cause for an extremely severe tetanic contraction of the entire abdominal wall.

It was Kussmaul who, in his famous article on the treatment of gastric dilatation by means of the stomach-pump, first described the occurrence of muscular spasm with pyloric stenosis. In some of these cases we have to deal with true tetany, which, as is well known, is characterized by increased mechanical and electrical irritability of the nerves and muscles. Other cases only resemble tetany, or else are epileptiform convulsions with loss of consciousness. The cases described by Kussmaul were pyloric stenoses, in which the frequent vomiting of large quantities of fluid led to a high degree of emaciation and decrease in the quantity of urine. He attributed the convulsions to the diminution of water in the organism, which was brought about by the vomiting of such large quantities of fluid and which led, as he reasoned, to the drying out of the nerves and muscles. This theory was not considered entirely satisfactory. It was claimed that there are other diseases of the gastro-intestinal tract in which an abundance of water is lost without the advent of tetany, and that in cases of tetany the introduction of water into the rectum did not prevent the attacks. Other explanations were, therefore, looked for.

Germain Sée believed that the convulsions were caused reflexly by the irritated nerves of the gastric mucosa. This so-called "reflex theory" explains only how the convulsions are brought on, without mentioning the predisposing element. We must remember,

however, that the exciting cause, which may be of various characters, is only a secondary element; in order to bring on a tetanic attack a change in the irritability of the nervous system is required and is really the underlying cause of the whole trouble.

This predisposing element finds more consideration in a third hypothesis, which, thoroughly in accord with modern teaching, attributes the origin of the attacks to autointoxication. This theory is mainly advanced by French authorities, who assume that decomposition-products are formed in the stagnating stomach contents, which, when absorbed, act deleteriously upon the nervous system, and in this way lead to attacks.

However, in spite of diligent research, no one has yet been able to demonstrate such poisons, and Friedrich Müller, a supporter of the reflex theory, points out very correctly that tetany appears, not in cases where the fermenting stomach contents are finally absorbed, but only in those in which the stagnating masses are removed from the system either by vomiting or lavage.

Since the removal of great quantities of fluid from the body is actually the only objective finding which is regularly observed in these cases, it remains, after all, the most important point, and if properly interpreted, gives us a better insight into the origin of tetanic attacks than the purely hypothetical autointoxication theory.

Thus, going back to Kussmaul's first explanation, we must say, as this keen observer rightly maintained, that the great loss of fluid by vomiting or lavage brings about the changes in the system which cause the tetanic attacks. We would add, however, that these discharges deprive the system not only of large quantities of fluid, but also of large amounts of chlorides. For in these cases of gastric dilatation complicated with tetany we often find enormously increased gastric secretion. Since, as we have seen in the beginning, the pyloric stenosis prevents the excessively secreted gastric juice from passing into the intestine, it is removed by vomiting or lavage, and thus great quantities of hydrochloric acid become lost from the system instead of being again resorbed.

Bouveret and Devic claim that gastric tetany is observed exclusively in such cases of pyloric stenosis as are accompanied by excessive hypersecretion. This is not absolutely true. Though the instances are very rare, Fleiner, for example, reports cases in which no increase of gastric secretion was found. We will not investigate now the cause of tetany in these particular cases. Suffice it to say that in gastric tetany, as is the case with other spasms, different factors may contribute to the development of the attacks. In the majority of cases, however, it is a fact that large quantities of chlorine are lost from the body by the removal of the excessively secreted gastric juice. This is proved by the fact that in these cases the secretion of chlorine through the urine steadily diminishes, and finally ceases altogether.

To be sure, the disappearance of chlorides from the urine here is not an absolute indicator of the quantities really lost from the body. The organism holds on to its chlorine obstinately. When we limit the supply of chlorine by cutting it out of the food the quantity excreted in the urine becomes less, and finally disappears altogether. At the same time the secretion of hydrochloric acid with the gastric juice will stop, as was shown by A. Cahn in his experiments on dogs. The organism saves its chlorine by checking its secretion. In spite of the diminished secretion, there may still be a great deal left in the system. In gastrosuccorrhœa, however, the conditions are altogether different. Through the constant irritation to the mucosa here, causing the excessive secretion of gastric juice, large quantities of chlorine are constantly withdrawn from the blood, and since they are removed from the body by vomiting or lavage, reabsorption is prevented, so that the body suffers an actual loss of chlorine. At the same time these patients do not take the proper amount of food, and, therefore, not the proper amount of chlorine to make up for the loss. In other words, there is increased excretion of chlorine, and the amount ingested is decreased—a unique pathological condition which must lead to an impoverishment of chlorides in the system. We may well assume that this diminution of chlorine plays some part in the development of tetany.

In looking through the literature I find that Korszynski and Jaworski as early as 1891 already regarded the decrease of chlorine in the tissues as the probable cause of gastric tetany. It is remarkable that this view can nowhere be found quoted in the text-books, in the special articles on gastric tetany by Fleiner, Albu, and others, or in Frankl-Hochwart's monograph "On Tetany," in Nothnagel's series. Yet their theory is of great assistance for the treatment of that peculiar and dangerous condition.

Korszynski and Jaworski, following their theory, recommended the injection of large quantities of normal salt solution, subcutaneously or by rectum, in order to overcome the chlorine starvation in cases of gastric tetany.

Tetanic attacks are of serious import, and often lead quickly to a fatal issue. In the latest summary by Albu of these cases, forty in all, there were thirty-one deaths—*i. e.*, $77\frac{1}{2}$ per cent. mortality. Their presence influences unfavorably the prognosis of an opera tion, and no operation should be undertaken in these cases before infusing large quantities of salt solution. This was done in our case before and after the operation, and it probably helped to bring about the favorable result, despite the presence of a perforation. To be sure, there were two other factors which favored the case: first, that the operation was performed only a few hours after the perforation; and, again, that the stomach had been washed shortly before the perforation occurred, thus preventing gastric contents from getting into the peritoneal cavity.

Albu claims that therapy offers no remedy which can either check or prevent a recurrence of the tetanic attacks. But, perhaps, as has been said before, it may be possible to end the attack by means of salt infusions. A recurrence can only be prevented by removing the cause. Their cause is, as we have seen above, motor insufficiency and the spastic or organic pyloric stenosis which hinders the passage of the more abundantly secreted hydrochloric acid into the intestines, thus preventing its reabsorption and depriving the system of large amounts of chlorine. In order to remove the cause the treatment should therefore be directed, first of all, against the motor disturbance. Whenever it is impossible to correct the motor insufficiency by internal means, it should be overcome by operation, either by pyloroplasty, gastroenterostomy, or resection, as the individual case may require. That is the rational treatment for gastrosuccorrhœa, as well as for tetany.

CHRONIC GASTRITIS DUE TO ALCOHOL.

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In the large cities we are accustomed to see numerous cases of gastric disorders which can be traced directly to excessive and habitual use of alcoholic beverages. These maladies are very common in the low orders of society which make up the mass of hospital patients, and it was from this prominence of these affections that we became interested in them. It is, of course, well recognized that alcohol can produce a chronic gastritis, but the clinical differences of gastritis due to alcohol from gastritis of other causes is not at present so clear. At present we are concerned only with the secretory disturbances of the gastritis of alcohol. The methods of work were those ordinarily used in the routine examination of gastric contents, Ewald's test-breakfast of bread and unsweetened tea being given in the morning and expressed thirty minutes or an hour later. Free HCl was estimated by titration with $\frac{n}{10}$ NaOH, using dimethylamidoazobenzol and Günzborge reagent as an indicator, and phenolphthalein as an indicator in estimating the total acidity. Lactic acid was always tested for, as were the gastric enzymes.

The cases seen divide themselves into two classes: those presenting symptoms of gastritis and those without such symptoms. Of the first class but little need be said. The symptoms are familiar: nausea, with retching, on rising in the morning, and the vomiting, perhaps, of some mucus. These symptoms pass away after a couple

of "drinks" to settle his stomach; then he is able to eat his breakfast, and is free from discomfort until the next morning. The gastric motility in these cases is considerably accelerated. The test-meal must usually be removed after forty-five minutes, at longest, in order to recover sufficient material for analysis. There is much mucus present, both free and mixed with food. Free HCl is usually absent. Total acids are low. Pepsin and rennin normal. The following case may be given as typical:

CASE XXI.—Man, aged thirty-four years; clerk. Family history and past history unimportant. Habits: drinks considerable whiskey; always a glass before breakfast. For last month or two the patient thinks he has averaged about one quart of whiskey per diem.

Present Illness. Has felt run down for some time, but with no special symptoms, however, except morning vomiting for several weeks. Ankles swell slightly, and is puffy under the eyes in the morning. No pulmonary, cardiac, or urinary symptoms.

Physical Examination. Normal, except for slight swelling of ankles. Urine: specific gravity 1024; no albumin or sugar; no casts.

Gastric Analysis. Ewald test-breakfast. Free HCl, 0; total acidity, 22; no lactic acid; enzymes present. Second analysis two days later shows same results.

The second class of these cases, those presenting no gastric symptoms, is of greater significance. The cases observed by the writer entered the hospital because of some malady other than gastric affections, and were recognized as possible cases of alcoholic gastritis on account of their habits or on account of the general alcoholic appearance. It was only after studying a number of the cases of chronic gastritis with pronounced symptoms that our curiosity was aroused concerning the gastric condition of those individuals who habitually use large amounts of alcoholic beverages, yet present no symptoms pointing to gastric disturbances. Hoping to obtain some light on this point, it has been our custom to make the routine gastric analysis on all of those cases that came into the hospital for any cause and whose appearance or history pointed to overindulgence in alcohol. The number of cases seen is now sufficiently large to permit of fairly accurate deductions. In contrast to the first class of cases there is no hyperkinesis, nor is there usually a great excess of mucus. The acid secretion being wherein morbidity is displayed, free HCl is always low, often absent, and in no case over 15. The average for our series is 5. The total acids are lowered, but not below the low normal limit. In other respects the gastric functions appear normal. The interest in these cases is mostly scientific, but there is, however, a practical application, namely, that one must be guarded in placing stress on the absence of free HCl in the diagnosis of stomach diseases unless free indulgence in alcohol can be excluded. The diagnosis of carcinoma

of the stomach in the early stages is based upon a number of small data, the most significant of which is, perhaps, the continued absence of free HCl. The point to which the writer wishes to call attention is that in these cases of possible carcinoma without definite signs or symptoms a history of alcoholic habits casts great doubt on that diagnosis. A case of the kind may be cited:

G. W., male, aged forty-eight years, entered the hospital complaining of weakness, loss in weight, and indefinite and occasional distress in the epigastrium. History and physical examination pointed to no organic disease. Blood count, normal. Gastric analysis showed absence of free HCl (three analyses). No diagnosis could be made, and an exploratory operation was done, which disclosed a small tumor in the tail of the pancreas (possibly carcinoma); the stomach appeared normal. There appearing no cause for the absence of free HCl in the gastric analyses, the man was later questioned concerning his habits. He had always drunk two glasses of whiskey before breakfast, he stated, and occasionally a glass during the day.

Riegel, Ewald, and other observers have pointed out the relation of alcohol to chronic gastritis; we are able to find no references, however, to indicate that there is recognized a change in gastric secretion due to alcohol previous to the excitation of subjective symptoms. Such a change as we have described is not accurately a gastritis chronica because, while there is slight increase in the mucous secretion, it is not marked nor constant enough to bring the syndrome under that head. It is, however, the precursor of that condition; and its interest in differential diagnosis, we hope, will lead some one to confirm our results.

A DIFFERENTIAL STAINING OF THE BLOOD WITH SIMPLE SOLUTIONS.

By William Page Harlow, M.D.,
of Boulder, Colorado.

For the past year and a half the writer has been practically in daily use of some one of the methyl-alcohol-eosin-methylene-blue blood stains (Jenner, May, Grünwald and Wright's), and has experienced trouble at different times in obtaining a methyl alcohol that would, with one of the above powders, give results as satisfactory as with previous batches. Neither are the ready-for-use fluids furnished by the chemists uniform and always satisfactory in result. He believes this experience to be a common one with hæmatologists and physicians who are doing any considerable amount of blood work. Therefore, it seems permissible to call attention to a method

giving a color picture similar to and recommended over the above because of:

1. The simple and less expensive solutions employed.
2. The easy technique and rapidity of staining.
3. The more uniform results obtained with stains and alcohols furnished from different manufactories and at different times.[1]

The solutions used are:

No. I. Eosin, 1 gram, in absolute methyl alcohol, 100 c.c.

No. II. Methylene blue, 1 gram; in absolute methyl alcohol, 100 c.c.

The procedure is:

1. A fresh-spread cover-glass (or slide) taken in the usual manner.
2. Dried in air only.
3. Preparation, held in self-closing cover-glass forceps, covered with as much eosin as it will readily hold without draining, allowing same to remain one minute.
4. Eosin rapidly decanted (shake off the surplus). Do not wash the spread in water, and do not allow it to become dry by evaporation.
5. The eosin moist specimen quickly covered with the methylene-blue solution, allowing to stand about one and one-quarter minutes (different blues require a few seconds more or less than this).[2]
6. Wash gently in ordinary pure water (best to wash or dip spread in a glass of water, rather than in a strongly running stream from tap).
7. Dry between layers of filter-paper and mount in balsam.[3]

The microscopic differential color picture shown by this method with the blood spread is as follows:

The Red Cells.

The hæmoglobin-holding cells, when normal, are a deep red, clean and evenly stained.

[1] The greater part of the work done by the writer was with Grübler's Pure French Eosin, the "B" Patent Methylene Blue, med. pur., and an absolute methyl Alcohol made by C. F. Kahlbaum, Berlin. Though recent experiments with other foreign-made stains, and an Eosin and a Methylene Blue furnished by Bausch & Lomb, and absolute Methyl alcohols furnished by Merck & Co., Eberbach & Son, Ann Arbor; E. H. Sargent & Co., Chicago, and Hynson & Westcott, Baltimore, have given quite uniform and very satisfactory results.

[2] It should be noted when the red blood cells are stained bluish that it is because of an understaining with the methylene blue, and that the eosin which is more or less loosely combined with the oxyphilic substances has not had sufficient time to neutralize the action of the methylene blue which has been added in excess. This variation in the time for counter-staining with the methylene blue has been found to be between one and one-quarter and two minutes in all the combinations that I have tried.

[3] Spreads dried in air may be kept unfixed, back to back, between folds of filter-paper for several months, and still give quite satisfactory staining results. A recent staining and examination of one-year-old unfixed spreads of malaria, leukæmia, and pernicious anæmia showed that the hæmoglobin-containing cell stained practically as well as when fresh—*i. e.*, anæmia, and all grades of polychromasia, nuclei, and the punctate basophilic granules of Grawitz are shown, as well as the malarial plasmodium. But in the colorless corpuscles the granules are not well differentiated, the nuclei, and basophilic substances only, being well brought out.

In the chloroses they are somewhat paler and show light to clear central areas.

In pernicious and other severe secondary anæmias, all grades of polychromatophilia, from terra-cotta, yellowish-brown, and greenish-yellow to a cloudy blue or purple are shown.

Small basophilic granulations are sharply brought out, being blue to deep purple in color, and found in cells the cytoplasm of which may show any grade of polychromatophilia.

The nuclei are deep blue, and, in the larger forms especially, the chromatin threads are clearly brought out.

The plaques, both in and out of the cells, are stained a lavender to dirty purple (but for the better study of the plaques, the simple staining of the unfixed spread for fifteen to thirty seconds with the methylene-blue solution alone is recommended. This is also good for all basophilic substances).

In the malarial plasmodium the cytoplasm is stained a bright light blue; the chromatin a deeper blue to purple; the segment walls are nicely shown, and the pigment appears as black dots or ovals.[1]

The Leukocytes.

Of the colorless polymorphonuclear granulated corpuscles, the neutrophiles generally show three or more quite dark-blue nuclei. The cytoplasm, taking a reddish tinge, is thickly studded with small violet to reddish granules, the whole apparently closely limited, as though by a cell membrane.

The oxyphiles, in a thickly spread blood specimen, are smaller than the neutrophiles, but in a thinly spread film usually appear larger than the neutrophiles. The nuclei, when there are three or more, as is often the case, are of the size and shape and stain the same as the nuclei in the neutrophiles, but more frequently there are two nuclei, oval or biscuit shaped, lying well apart in the cell, which are larger and stain a paler blue than the neutrophiles. The cytoplasm has a red tinge, if any, and is more or less loosely studded with large, glistening, rose-red granules that do not seem to be closely restrained, some often overlying the nuclei, others being entirely without the normal limits of the cell (the so-called "explosive" action after the drawing of the blood).

The basophiles generally are a little smaller than the neutrophiles, but vary in size to as large as the oxyphiles. The nuclei are often hard to differentiate from the cytoplasm, both being stained a pale blue. In some cases the nuclei are stained a deeper blue than the cytoplasm, are irregular in shape, and often eccentrically placed. But the coarse, spherical granules, varying in size from that of a

[1] The addition of one-half per cent. of sodium carbonate or lithium bicarbonate to the methylene-blue solution will give a better stain for the malarial plasmodium, but other structures are stained a little more blue than with the simple solution.

neutrophile granule to as large as fat-droplets, some staining a deep blue to purple or almost black, are distinctive.

The mononuclear granulated corpuscles or myelocytes stain about the same as the polymorphonuclear cells, having the same kind of granules. The nucleus is generally at one side and is round or oval, often showing two or more clear dots; and sometimes a fine reticular chromatin may be noted.

The neutrophilic myelocyte is the largest of this class. Its nucleus is large, often taking up more than half the cell, and is generally eccentrically placed. The cytoplasm is closely filled with violet-stained relatively small granules.

The oxyphilic myelocyte is a little smaller than the neutrophile. Its nucleus is stained a paler blue and generally shows little or no structure. The cytoplasm is of a reddish tinge, and the granules filling the same, sometimes partly overlying the nucleus, are large and quite uniform in size, and stain a glistening rose-red.

There appear to be two forms of the mononuclear cell, containing basophilic granules, though both may be of bone-marrow origin, and one an earlier form of the other.

The basophilic myelocyte (undoubtedly properly so classified because it is a mononuclear cell with basophilic granules, and can be demonstrated in normal and pathological bone-marrow) is a little larger than a polymorphonuclear neutrophile. It has a deep-blue staining nucleus located a little to one side of the centre. The cytoplasm is stained a lighter blue and is fairly well filled with basophilic granules about the size of the neutrophilic granules; these are stained a deep but real blue.

The other form, the origin of which has been attributed to the tissues and spleen, and classified as a mast-cell, is round or more often oval in shape, varying greatly in size—*i. e.*, from being but little larger than a red blood cell to as large as a neutrophilic myelocyte. The nucleus and cytoplasm are stained a pale blue and sometimes cannot be differentiated; others of these cells, however, will show a well-defined and cloudy to deep-blue staining, oval or lobulated nucleus. The cytoplasm is stained a pale, clear blue, and studded with deep blue to royal purple granules which differ somewhat in size and shape, but most of which are large and coarse, and oval, triangular, or cuboid in form.

The Non-granular Mononuclear Corpuscles.

The small lymphocyte is about the size of a red blood cell and stains in at least three different ways, under apparently normal conditions, and in the same specimen.

With this staining method, in one form, we see a small, nearly round cell with a relatively large pale-blue staining nucleus which may show two or more pseudonucleoli and a small amount of

chromatin. The nucleus is apparently nearly surrounded by a crescent of cytoplasm which exhibits a band of reddish staining cytoplasm next to the nucleus, then outward from this a pale-blue shading to a dark-blue periphery, or the dark blue contiguous to the red.

In a second form this surrounding cytoplasm seems curled or pressed up around the nucleus, and we see a pale-blue nucleus surrounded by a very narrow band of deep-staining cytoplasm.

In the third form the cytoplasm seems to almost or entirely surround and cover the nucleus, and we get the same-sized cell, dark-blue staining, with nucleus usually not apparent; but often nodal thickenings of the cytoplasm give the appearance of granules.

In some cases of lymphatic leukæmia, where there is a great proliferation of these small lymphocytes, we may see a majority of the cells with the nucleus staining a hazy blue and the cytoplasm tinged with blue, or nearly clear.

The large lymphocytes are the size of or larger than a polymorphonuclear neutrophile. They have a larger nucleus and an absolutely and relatively larger amount of cytoplasm; otherwise the description of the first form of small lymphocyte will suffice, and in general they may be classed together.

The large mononuclears and transition forms may be considered together. They have a structureless light-blue staining nucleus, round or more often oval or indented (as kidney shaped), and with a relatively large amount of cytoplasm, which often is not stained and is barely discernible. In this there may be vacuoles and nodal thickenings, but no granules.

In a series of specimens lately examined, a number of cells that, with other staining methods, would have been classified as "large mononuclear" or "transition forms," showed the double coloring of the cytoplasm, and it seems quite probable that they are merely other forms in the chain of the lymphocytes.

There remain to be noted a group of mononuclear cells, product of the bone-marrow, and being either by-products (dying) or young cells intermediary in stage between basic cells and the corpuscles of peripheral blood. These have been noted as marrow cells (mark-zellen), stem cells (stamm-zellen), an earlier form of the mark-zellen and stimulation or irritation forms (Reizungsformen). These can be well classified together under the head of marrow cells. These are round cells about the size of the polymorphonuclear neutrophile. They all react to basic dyes only. In the young forms a nucleus is not noted, but we see a round cell staining quite deeply blue, being darker at the periphery. In this cell is a rough protoplasm having a "ground-glass" appearance, often two or more nucleoli or areas appearing vacuolated; and perhaps some granuloid areas due to thickened cytoplasm. In later stages a nucleus staining a little deeper blue than the surrounding cyto-

plasm is seen, otherwise with the same appearance as in the first stage.

In still later stages the cytoplasm may begin to take on a violet or reddish hue, and granules begin to appear, when we must class the cell as a myelocyte. All grades between the diffuse-looking stamm-zellen and the fully granulated myelocyte may be noted.

ON THE MECHANISM OF THE CONTRACTION OF VOLUNTARY MUSCLE OF THE FROG.

By Edward B. Meigs,
of Philadelphia.

As a first step in the search for a mechanical explanation of muscular contractility, it is necessary to have a definite idea of the change of form which takes place in a muscle fibre when it contracts. For various reasons I have used frog's voluntary muscle in nearly all of my experiments. It is well known that when a fresh frog's muscle is placed in distilled water it goes into a state

Fig. 1.

Muscle fibres in water rigor.

of complete and lasting contraction called water rigor. If a muscle in water rigor be carefully teased, some of its fibres will generally be found in the condition shown by Fig. 1.

Fig. 1 is a drawing of two fibres from a frog's sartorius in water rigor. The drawing was made with the camera lucida, and the outlines are, therefore, as true to nature as possible. The upper fibre

has been bent almost into a circle by the teasing, while the lower one is nearly straight. The specimen from which Fig. 1 was drawn was prepared as follows: The sartorius was dissected from the thigh of a freshly killed frog and placed in distilled water for about ten minutes. It was then carefully teased in a little water on a glass slide, the excess of water was removed, and a drop of glycerin applied. The preparation was then covered with a cover-glass, which was cemented to the slide with asphalt. The teased fibres were examined under the microscope in water before the glycerin was applied, and they were then seen to present the same appearance as in the drawing, except that the distended portions of the lower one were as symmetrically globular as those of the upper one in the drawing. I do not know why the glycerin caused the irregularity of outline of the lower fibre without affecting the upper one.

I have treated a number of muscles in the manner described and I have almost always been able to obtain some fibres from each muscle in the beaded condition illustrated; but in no case have I found more than a small proportion of the fibres of a muscle in this state. The following, however, will show that the beaded is the true form of contracted muscle.

It is universally acknowledged that the contraction of muscle under electrical stimulation is the same as the normal contraction, and, therefore, if fibres can be shown to take the form of Fig. 1 when they contract under electrical stimulation, it must be admitted that the beaded form is the normal state of contracted muscle. It is not easy to observe beneath the microscope the change of form which frog's muscle fibres undergo during contraction due to electrical stimulation. If the muscle is large enough to be dissected out without damage, it is too large to allow its fibres to be seen clearly through the microscope. On the other hand, the least roughness in handling a small muscle destroys the irritability of all or of nearly all of its fibres. Besides this, the change from the uncontracted to the contracted form is so rapid that it throws the fibres under observation out of focus, and the contraction lasts at most only a few seconds, affording little time to get them in focus again.

I have found the sartorius to be the best muscle for this experiment. It is thin and flat and its fibres are parallel. If this muscle be carefully dissected from the thigh of a small frog and laid across the electrodes so that it can be observed through the microscope, the straight outlines of the fibres and the cross-striations can be distinctly seen. If now the tetanizing current be applied, the fibres will probably fly out of focus. But if they are quickly brought back into focus, it will be seen that their outlines are no longer straight, but that they have taken the beaded form.

After a muscle lying on a pair of electrodes with its ends unattached has been thrown into tetanus, it never again completely relaxes,

but remains shorter and wider. This can be distinctly seen if the muscle be watched with the naked eye, and the fact is a great help in the observation of contraction. For, after the first application of the tetanizing current, the fibres, being already partially contracted, move to a much less extent with each subsequent application, and remain in focus, provided the objective used be of reasonably low power. If the tetanizing current be weak, and if it be applied for only short periods, the fibres may be seen with the microscope to contract and relax again and again, and the beading of the fibres can be seen to increase when the current is applied, and to diminish when it is removed. Of course, this beading of the fibres under electrical stimulation can only be seen at the cost of a good deal of care and trouble. I have again and again been disappointed by finding that the irritability of the fibres under observation has been completely lost; but I have repeatedly observed the increase and diminution of the beading on application and removal of the tetanizing current, and I have never seen a mere broadening of the fibres on application of the current and a narrowing on its removal.

It must be said, in passing, that the constrictions and bulgings of the contracted fibres cannot be regarded as "waves of contraction." As the bulgings do not entirely disappear on removal of the tetanizing current, it can easily be seen that they always occur at the same points. This seems to show that they are caused by definite structural peculiarities of the fibre. Moreover, the bulgings remain stationary during the flow of the current. It is impossible to conceive a stationary wave of any sort, and equally impossible to believe that "waves of contraction" could be present during tetanus, which is a state of complete contraction throughout the length of a muscle fibre.

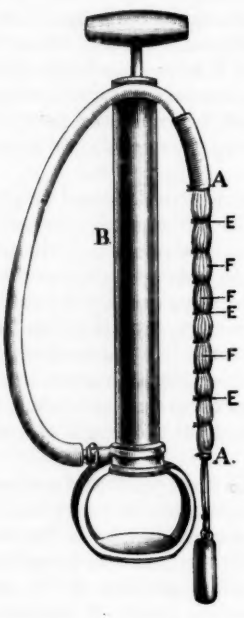
It is, of course, difficult to observe the finer peculiarities of muscle fibres in tetanus. A whole muscle is an unsatisfactory object for microscopic examination, and the tetanus can last but a few seconds at most. As far as I have been able to discover, however, the appearance of fibres in tetanus is similar to that of the beaded fibres illustrated by Fig. 1. The important points of similarity are the disappearance of the cross-striæ and the great distance between the contiguous constrictions. The portion of a muscle fibre between two contiguous constrictions evidently contains many cross-striations, for the distance between two contiguous striæ is not more than a tenth of the diameter of the muscle fibre, whereas the distance between two constrictions is nearly equal to the diameter of the contracted fibre at its widest part.

It may be that observations similar to mine have been already recorded, but I have examined a good deal of the literature of the subject and have not been able to find any reference to the fact that frog's voluntary muscle fibres take the beaded form when

they contract. Ranvier,[1] however, mentions the fact that the fibrils of insects' wing muscles often present the beaded appearance. But whether the facts have been recorded or not, they demand more consideration than they have hitherto received.

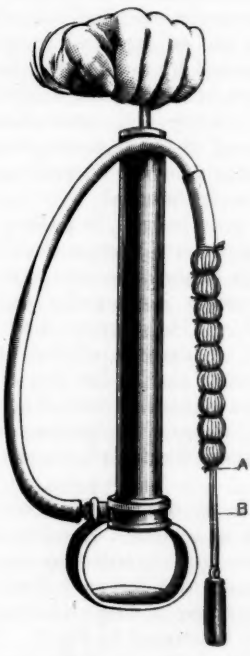
I shall now give what seems to me the most probable explanation of contraction. It is based partly on the observations recorded above, but the correctness of the observations is not affected by the probability or improbability of the explanation. I shall begin by showing that if the muscle fibre be assumed to have a certain mechanical

FIG. 2.



Fibre model.

FIG. 3.



Fibre model contracted.

structure, the phenomena of water rigor may be explained on perfectly well-known mechanical and physical principles. I can best describe the structure by exhibiting drawings of a model.

Fig. 2 represents a model supposed to have the structure of a muscle fibre. *A A* is a tube of thin rubber, encircled at intervals by wire rings, *E E E*. Along the tube run inelastic cotton threads, *F F F*, each of which is attached to all of the wire rings. *B* is an

[1] Leçons d'anatomie générale sur le système musculaire.

air-pump, by which air can be forced into the tube *A A*. When this is done the model takes the form shown by Fig. 3. Each of the divisions of the tube between the wire rings tends to become spherical, the cotton threads are thrown into curves, and, as they are nearly inelastic, the whole structure necessarily shortens. The illustrations are reproduced from photographs of the model taken at equal distances from it, so that the relative dimensions are preserved; the distance between the lines *A* and *B* (Fig. 3) represents the amount of the shortening.

It will be necessary now to return a step and consider what are the most obvious changes that take place when a fresh frog's muscle is placed in distilled water. These changes may be summed up as follows: The muscle absorbs water, it contracts, and its fibres change from the cylindrical to the beaded form. It may be proved that the muscle absorbs water by weighing it before placing it in the water and afterward. It will be found to be heavier afterward. The contraction of the muscle is remarkable in several ways. It is very slow, for about fifteen minutes elapse before it is complete; it is almost exactly equal to the greatest contraction that can be obtained with the tetanizing current; and once complete it lasts indefinitely.

The absorption of water by the muscle may be explained by the laws of osmosis. The shortening of the fibres and their change of form are immediately explained if they are supposed to have a structure mechanically equivalent to that of the model. For if they had this structure, the water passing into them by the osmotic process would compel them to change from the uncontracted cylindrical form to the contracted beaded form, exactly as air forced into the model compels it to change from the form shown by Fig. 2 to the form shown by Fig. 3. When the osmotic process is complete there is no tendency for it to reverse itself, and the muscle therefore remains contracted for an indefinite time.

There is one mechanical fact which greatly strengthens the argument. It is a necessary part of the construction of the model that the distance between the wire rings should bear the same relation to the diameter of the tube as shown by Fig. 2. Suppose that all of the wire rings except those at the top and at the bottom of the tube were removed, and that the threads and the rest of the machine were left as before, a much greater amount of air would then have to be forced into the tube before the curvature of the threads and consequent shortening of the model was as great as in Fig. 2; for the whole tube would tend to take the form of a sphere, and before it could assume this shape the rubber at the middle would have to stretch enormously, and the diameter at that point would be very great. On the other hand, practically no shortening can be produced in a machine with its rings much nearer together than those of the model (Figs. 2 and 3). It is a striking coincidence that the

constrictions of the fibres in Fig. 1, the constrictions of frog's fibres in electrical tetanus, and those of the fibrils of insects' wing muscles are all at just such distances that the greatest amount of shortening can be obtained with the least expansion in volume and with the least stretching of the fibre sheath.

The four preceding paragraphs may be summed up as follows: All of the phenomena of water rigor may be explained on perfectly well-known mechanical and physical principles, if it be assumed that the muscle fibre has the same structure as the model shown by Figs. 2 and 3. It is known that water passes into the fibres by osmosis while the muscle is going into water rigor, and if the fibres have the structure in question, this passage of water into them is sufficient to cause both the change of form and the shortening. As the phenomena of water rigor can be explained by so simple an assumption, I have thought it justifiable to make the assumption.

The fact that so few of the fibres of a muscle in water rigor can be found in the beaded condition is, of course, a strong counter-argument, but it must be remembered that distilled water is a reagent extremely destructive to muscular tissue. If the antenna of a living fresh-water snail be cut off near its base it will immediately contract. If it be then examined under the microscope in a little water, constrictions and bulgings are seen, not unlike those of the contracted muscle fibres. After a quarter of an hour the constrictions become much shallower and fainter, although the total length of the organ remains unchanged; and after half an hour or an hour they completely disappear. It seems quite possible that the constrictions of the muscle fibres are acted upon by the water in the same way as those of the snail's antenna. When it is added that fibres in electrical tetanus invariably present the beaded appearance, the fact that many fibres from muscles in water rigor do not present that appearance becomes insignificant.

If my explanation of water rigor is correct, it suggests very important conclusions. The structure which I have attributed to the muscle fibre is a highly specialized one, and it is apparently designed for the purpose of producing contraction. Besides this, it evidently acts when a muscle is thrown into tetanus by the electrical current, for fibres in tetanus exhibit the beaded form. The conclusion is inevitable that the structure in question is part of the mechanism of contraction.

To produce contraction in a structure like the model, it is necessary to increase the volume of the contents. There are only two ways in which this increase could be accomplished in muscle fibres. Either the contents of the fibres might expand or fluid might pass into the fibres from without. If contraction were caused by an expansion of the contents of the muscle fibres, it would necessarily be accompanied by an increase in the volume of the muscle. But it is known that the volume of a muscle does not increase during

contraction, and it cannot, therefore, be supposed that contraction is due to the expansion of the contents of the muscle fibres. If, therefore, the muscle fibre contracts in the same manner as the model, it is necessary to suppose that its contraction is caused by the passage of fluid into it from without.

It is thus seen that a consideration of the phenomena of water rigor and of the change of form which frog's muscle fibres undergo during contraction leads to the conclusions that the fibres have a certain mechanical structure which causes them to contract when the volume of their contents is increased, and that the ordinary contraction of muscle is caused by the passage of fluid from the spaces between the fibres into the fibres. (For convenience, I shall hereafter call the spaces between the fibres the interfibrous spaces.) It may be asked whether this conclusion in any way helps to explain muscular contraction. I believe that it does, for the passage of fluid from one part of an organ to another is a process which is quite likely to be explained on the principles of inorganic chemistry. There are several analogous processes, such as diffusion and osmosis. And besides this, the passage of fluid from one part of an organism to another is probably the most widely distributed and elementary process in the organic world. Plants universally receive their nourishment and grow by this process; it may be observed in the amœba during the extrusion of a pseudopod; and in the higher animals it takes place in the digestive tract, in the vascular system, in the kidneys, and in all of the glands. Not only this, but there is good reason to believe that this process is the cause of the movements of the insectivorous plants[1] and of Mimosa pudica.[2]

The points of similarity between muscles and glands have received some notice from physiologists. Rosenthal mentions these similarities in the work quoted above (see pp. 212 and 213). They are: first, the fact that both muscles and glands are thrown into action by stimulation of their nerves, and, second, certain likenesses in the electrical reactions. The following experiment seems to show a striking histological similarity. If one of the voluntary muscles be dissected from a freshly killed frog and immediately frozen and cut into thin transverse sections the sections present the appearance of Fig. 4, which was drawn from such a section with the camera lucida.

The striking part of the appearance of Fig. 4 is the segmented ring of darker tissue which surrounds each of the fibres, and which resembles a layer of secreting cells. The fact that transverse sections of muscle prepared by the freezing process resemble sections of glandular tissue supports my hypothesis in the following manner: I have been endeavoring to show that the contraction of muscle is due to the passage of fluid from the interfibrous spaces into the

[1] Charles Darwin. On Insectivorous Plants, London, 1875, second thousand, p. 255.
[2] I. Rosenthal. General Physiology of Muscles and Nerves, London, 1881, pp. 2 and 3.

fibres. The activity of a gland is secretion, which consists in the passage of fluid from the interacinous spaces into the acini, whence it is discharged through the ducts. In other words, according to my hypothesis, there is a fundamental likeness between the function of a muscle fibre and the function of a gland acinus. And if, in addition to this, there is a strong histological likeness between the two tissues, the fact constitutes a considerable addition to the argument.

The appearance of Fig. 4 can always be obtained by the following method: A frog is killed, the sartorious is dissected out, frozen, and cut into sections without being put in any reagent, and all this is done as quickly as possible. The sections may be floated out in a 0.6 per cent. sodium chloride solution or in distilled water and examined with the microscope. They will then be seen to

FIG. 4.

Cross-section of muscle prepared by the freezing process.

have the appearance of Fig. 4. Such sections may be preserved in glycerin. Alcohol produces a great decrease of the sharpness of the appearance. In very warm weather it is necessary to cool the frog with ice before killing it, and to dissect out the muscle and freeze it even more quickly than in cooler weather.

Whether the appearance presented by Fig. 4 or that of sections of muscles which have been preserved in alcohol or some other fixative, and have then been mounted by the paraffin or celloidin method, is more truly representative of the condition of frog's muscle during the life of the animal must be left to the judgment of scientific men. The answer to the question will depend on the answers given to two subordinate questions. First, Is the freezing process or is the alcohol and paraffin process likely to be more destructive? Second, Is the appearance of Fig. 4 or that of sections prepared by the alcohol and paraffin process more suggestive of mutilated tissue? In discussing the first question it must be said that frog's muscle may be frozen and melted again and immersed for a considerable period in 0.6 per cent. salt solution without losing its irritability.[1] The process by which the appearance of Fig. 4 is obtained can be completed within ten minutes of the death of the animal from which the tissue is taken, and no reagent capable

[1] American Text-book of Physiology, Philadelphia and London, 1901, 2d ed., vol. ii. pp. 58 and 162.

of destroying the irritability of the tissue is used. On the other hand, the alcohol and paraffin process requires many days for its completion, and any one of the reagents used is capable of destroying the life of the tissue.

It is difficult to discuss the question whether the appearance of Fig. 4 or that of alcohol and paraffin sections is more suggestive of mutilated tissue. Every histologist feels capable of judging from appearance alone which of two specimens of the same tissue is the more perfect, and yet it would be difficult for him to say on what he based his judgment. The distinctness of the outlines and the amount of differentiation in each of the specimens are, perhaps, the most important points to be considered. The sections illustrated by Fig. 4 certainly show more differentiation than the alcohol and paraffin sections. In Fig. 4 the fibres appear to be made up of two distinct parts, the central disk and the peripheral ring, and the latter is evidently divided into segments. In the alcohol sections each fibre appears as a nearly homogeneous disk. It is easy to imagine that the mutilation of a tissue whose true appearance was that of Fig. 4 might produce the appearance of the alcohol sections; but difficult to suppose that the mutilation of a tissue whose true appearance was that of the alcohol sections might produce the appearance of Fig. 4.

There is one difficulty which must be briefly considered before the conclusion of this discussion, namely, that the action of muscle is extremely rapid, whereas the process of the absorption of fluid is commonly regarded as a slow one. But the unusual conditions under which absorption takes place in muscle must be kept in view. The largest muscle fibres are in reality the merest threads, each of them is entirely surrounded by fluid, and there is, therefore, in every muscle a very large surface exposed by the fibres in comparison to the small amount of fluid to be absorbed by them. The finest cotton thread is exceedingly thick in comparison with even the largest frog's muscle fibre, and yet a cotton thread cannot be dipped in water for a fraction of a second without becoming saturated. The saturated thread has absorbed at least half its volume of water, and this is much more proportionally than would be required to cause complete contraction in a muscle fibre with the structure of the model. But a stronger argument can be adduced against the assumption that the contraction of muscle cannot be due to the movement of fluids because the fluids cannot be conceived to move sufficiently rapidly. If nothing further be conceded regarding the constitution of muscle than that it is composed of solids and fluids, it must be admitted that the fluids move whenever the muscle contracts; and the fluids could surely be moved by chemical processes as rapidly as by the movement of the solid parts of the muscle.

If I knew nothing further about muscle than that it was composed of solids and fluids and had the power of movement, it would

seem to me much more likely that the movement of the fluids caused the movement of the solids than that the movement of the solids caused the movement of the fluids. The former is the case in every machine made by man for the purpose of converting chemical into mechanical energy.

I realize that my conclusions are opposed to the latest results of scientific research, in so far as these seem to show that muscle fibres are composed of fibrillæ. If frog's muscle fibres are composed of fibrillæ, which are independently capable of contraction, the whole of the foregoing argument falls to the ground. I hardly dare to urge my own observations against those of such an authority as Rollett, and yet everything that I have seen seems to me opposed to the view that the muscle fibres are composed of fibrillæ. The appearance of the cross-section of frog's muscle, of which a drawing has been submitted, goes to show that fibrillæ do not exist in frog's muscle; and the beaded appearance of contracted fibres, whatever construction may be put upon it, seems to favor the idea that the fibre is the contractile unit. It may be urged that most of the work which tends to prove the existence of fibrillæ has been done with other muscle than the voluntary muscle of the frog, and the evidence favoring the existence of fibrillæ in frog's muscle is very unsatisfactory. It depends on the appearance of the muscle and on certain results to be obtained from specimens hardened in alcohol. Leaving aside the argument that appearance alone can never be a very satisfactory indication of mechanical structure, it must be conceded that the exact appearance of the interior of a fresh frog's muscle fibre is not very accurately known. Great amplification must be used to see the details of the structure which are supposed to represent fibrillæ, and with a high power little more than the upper surface of a thick frog's fibre can be sharply seen. As for the fact that frog's fibres may, after a long immersion in alcohol, be teased into much smaller fibrillæ, there is no evidence to show from which part of the fibre these fibrillæ come. They may be merely portions of the fibre sheath. And there is a good deal of direct evidence to show that the interior of fresh frog's muscle fibres is in a fluid or semi-fluid state.

Sir Michael Foster[1] mentions the classic instance of the nematode worm seen making its way through the centre of a fibre. And Rosenthal[2] says: "It can be shown that a muscle fibre when recently taken from the living animal must, in reality, be of a fluid, or, at least, of a semifluid nature. So that it is impossible to affirm that either the discoid or the fibrilloid structure actually exists in the muscle fibre itself; it must rather be assumed that both forms of structure are really the result of the application of reagents, which

[1] M. Foster. Text-book of Physiology, London and New York, 1891, 5th ed., part i., p. 95.
[2] General Physiology of Muscles and Nerves, London, 1881, p. 14.

solidify the originally fluid mass and split it up in a longitudinal or transverse direction."

It will probably be a long time before an adequate comprehension of the mechanism of muscular contraction is attained, and it is not to be expected that the subject could be completely elucidated within the limits of a single paper. I have simply pointed out the explanation which, after a consideration of the various facts, would seem to be the most likely one.

OBSTRUCTION OF THE CENTRAL RETINAL ARTERY.[1]

REPORT OF A CASE.

By William T. Shoemaker, M.D.,
of Philadelphia.

The question of embolism versus thrombosis of the central retinal artery has for a great many years been discussed and argued until it might be said to be almost threadbare; and, curiously enough, many of the best observers have titled their cases embolism, while declaring their belief in probable thrombosis. That this question is still an unsettled one in medicine is sufficient apology for further contributions.

The following case I believe to be one of lateral thrombosis of the central artery of the retina. The evidence to be adduced, though not conclusive, strongly favors such a diagnosis.

F. W., aged seventeen years, twister in a mill, came to the Eye Clinic of the German Hospital November 18, 1903, with history as follows: One week ago, while returning home from a matinee, she suffered a sudden attack of partial blindness in the left eye. This was described as everything becoming black before O. S., except in the lower field, where vision remained. Subjectively she noticed that the top of the head of a person looked at was not seen. The condition did not improve, but, on the contrary, she thinks became worse in the succeeding few days. The attack was neither preceded, accompanied, nor followed by vertigo, headache, or any physical discomfort whatever. An interesting event in the history of the attack which must be considered, though it is, perhaps, a little sensational, is the following: The play which she witnessed was an extravagant melodrama, in which the heroine, during the third act, became suddenly blind, and continued so until the end of the play, with dramatic effect. The patient was much impressed, and, as she expressed it, could not get the afflicted heroine out of her mind. While thinking of this accident, she had proceeded but three squares from the theatre when her own trouble commenced.

[1] Read before the Ophthalmological Section, College of Physicians, December 15, 1903.

Her family history is good. Her father and mother are living and well. She is the third of eight children, the oldest twenty-one years, the youngest three years; all living and healthy, except the seventh, who died in infancy. Her personal history is good. She had scarlet fever, measles, and whooping-cough in childhood; she has never had rheumatism, has no intestinal nor digestive disturbance; shows no evidence of syphilis, congenital or acquired. She menstruated at thirteen and has done so normally since. Two years ago she had typhoid fever, and was probably quite ill. At the present time she is well developed, of good color, and apparently well balanced. She seems to be in no way neurotic. She experiences some shortness of breath after sudden exertion, such as running up stairs.

Dr. Henry F. Page examined her heart November 27th; in his report he states: "Patient well nourished, color good, mucous membranes normal in appearance. Radial pulse soft, receding, and slow. Pulse rate 63. Inspection of chest shows slight bulging of left side, due probably to a slight degree of lateral curvature. Apex-beat not visible, but determined normal by palpation and auscultation. Slight pulsation of vessels of the neck. Fine thrill felt over carotids. Soft, blowing, systolic murmur heard at aortic and pulmonary orifices transmitted to the carotids." As a result of his examination, he believes the murmur present to be functional in character.

A complete analysis of the urine was made in the chemical laboratory of the Medical Department, University of Pennsylvania, by Dr. John M. Swan. It is not necessary to read the figures; suffice it to say that the patient has nephritis, and is eliminating much less nitrogen, sulphates, and phosphates than normal. The albumin is less than 0.025 per cent. by Esbach's method; the casts are hyaline and very few in number. There is no sugar.

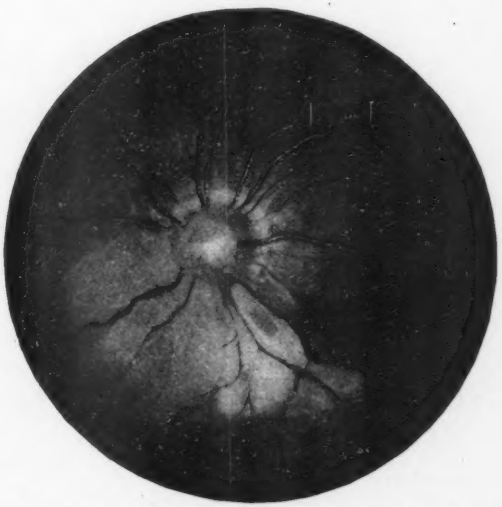
Upon admission, both eyes, conjunctiva slightly injected, pupils equal, irides freely active to light. Movements of eyeballs free in all directions. Central vision: O. S. (affected eye), 5/7.5. V. O. D., 5/5.

Ophthalmoscopic Examination. O. S., media clear disk margins everywhere blurred, but more so below. There is a diffused area of ischæmic infarction, mostly below, but especially marked in a localized patch about the size of the disk, situated 1 d. d. down and out. Into this patch runs an obliterated vessel from which has been a small extravasation. The lower temporal artery from its exit to a turn 1 d. d. from the disk is reduced to a thread; from there on it is of good size. A small branch from this artery running through the infarcted area is filiform, but peripherally recovers a normal diameter. Directly off the disk below are three small, indistinct, flame-shaped hemorrhages. Most of the arteries and veins are reduced in size; they all taper as they enter the disk, and many of them show a most irregular contour varying with diameters. The light streak on the smaller vessels is absent, and on the larger is diminished in

brilliancy, but continued far to the periphery. The light streak on a few of the upper ones is beaded. The vessels are nowhere tortuous, and peripherally they seem normal. The macular region shows a number of reflexes, streaked and radiating. The appearance here is granular, but there is no cherry-red spot. The porus opticus is enveloped in an impenetrable mist. Pressure on the eyeball causes a complete blanching of the disk, with not a vessel on the disk to be seen.

There is a little variation from the usual arrangement of the vessels. The majority of them, for instance, seem to come from the superior branch of the first bifurcation, there being at least seven from this source against three or four from the inferior branch. Among those

FIG. 1.



Obstruction of the central retinal artery. O. S., probably lateral thrombus.

first mentioned is a large artery running directly outward and curving above the macula, in close proximity thereto. This vessel, although it points to the lower retinal artery, probably belongs to the upper system because it passes above the macula and supplies the upper outer fundus.

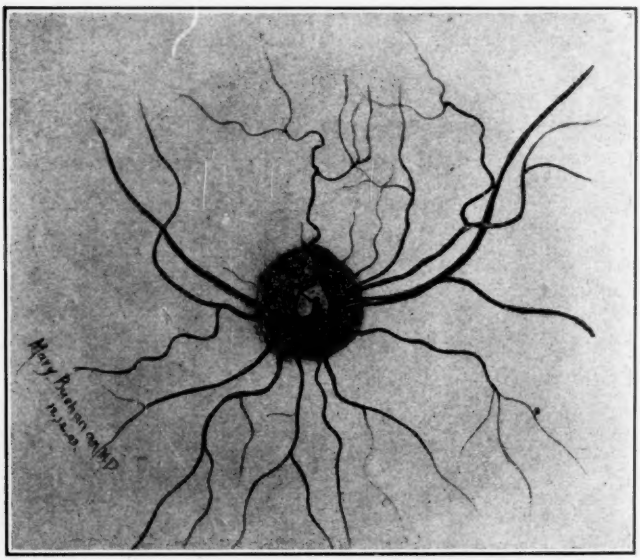
O. D. is normal ophthalmoscopically, but shows the same arrangement of the vessels. The upper fundus is much more vascular than the lower, and there is also a large macular artery, but in this eye it is a branch of the inferior system. There is in both eyes a tendency to lateral distribution of the vessels.

Dr. Buchanan, who has followed this case with me from the start, and who has been of great assistance in its preparation, has made

the water-color sketch, which shows well the condition about ten days after the attack. The rough sketch of O.D. shows the arrangement of the vessels in that eye.

Subsequent changes noted at intervals of two or three days have all been in the direction of increasing haziness of the retina (secondary œdema), enlargement of the veins and some increase in the diameter of the arteries. The small hemorrhages have disappeared. The infarcted area has become less pronounced by contrast. Vision gradually reduced until seven days after the first note it was 5/15. Since then it has improved, and at the present time it is 5/10.

FIG. 2.



Vascular arrangement of fundus. O. D.

November 25th. Two weeks after the attack a punctate deposit appeared on the posterior surface of the cornea, rather general in distribution, with a tendency to conical formation. This deposit has almost entirely disappeared. Fine vitreous opacities are now present. There has been no alteration in tension. The fields correspond to the fundus condition.

The clinical signs of thrombosis as given by Priestley Smith, in 1884 (*Ophthalmic Review*), and which might be said to have become classic, are:

(*a*) Previous attacks of transient blindness in the affected eye.

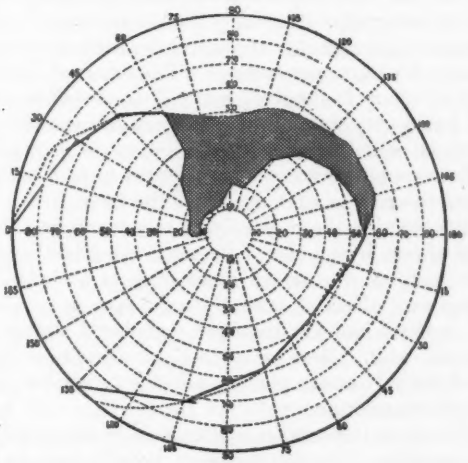
(*b*) Simultaneous attacks of transient blindness in the fellow-eye.

(*c*) Previous or subsequent attacks of transient blindness in the fellow-eye, especially if conditions of the attack were the same in the permanent as in the transient attacks.

(*d*) Signs of disturbance of the cerebral circulation at the onset of the blindness—dizziness, faintness, headache.

In the history of the present case there are no points of correspondence with the above, but investigation along other lines would seem to make questionable the necessity for any one of these signs in establishing a case of thrombosis. It is true that with these clinical signs the case is probably thrombosis, but, with any or all absent, thrombosis is not to be excluded. In other words, when positive they are strong, and when negative they are weak. This case has been

FIG. 3.



Field. O. S.

studied therefore more from the side of general medicine and general pathology than from the clinical.

There are three important causative factors in the coagulation of blood within the vessel wall during life, two or all of which are for the most part essential.[1] These factors are alteration in the blood current, changes in the vessel wall, and alteration in the blood.

Ludwig Gutschy, in a recent article in the *Beiträge* for pathological anatomy and general pathology, has arrived at conclusions as to thrombus formation which seem to be of service in considering cases such as the one here reported. The first change he declares is one of separation; the fibrin separates from the blood plasma, forming a jelly-like mass, which adheres to the vessel wall, and

[1] Stengel. Text-book of Pathology.

which he calls the *primary fibrin membrane*. Upon this membrane, which is sticky, leukocytes collect, the resulting mass being a white thrombus. T. Wharton Jones[1] has found that on pressing the neck over the artery or vein firmly with a blunt point, an agglomeration of colorless corpuscles, with a few red ones, held together apparently by coagulated fibrin, occurs, adheres to the wall of the vessel, and more or less completely obstructs it at that place.

Returning now to the three factors more or less essential for thrombosis; under the first, or alteration in the blood current, we have to consider anything which slows the blood current, such as weakness of the heart, narrowing of the bloodvessels, or pressure on the vessel wall. I think it can be demonstrated that the blood current in this case was very much reduced in velocity, especially in the central retinal artery. Normally the blood travels in the carotids from 300 mm. to 500 mm. per second, and in the very small arteries it travels but a few mm. per second.[2] The external diameter of the central retinal artery is about $\frac{1}{10}$ mm.; it is therefore a very small artery, and has a very small lumen. Dr. Page's examination shows the pulse to be soft, receding, and slow, with a rate of 63 per minute. His examination was made under the usual conditions which tend to excite the patient and accelerate the heart-beat. If now the velocity of the blood in the radial artery is reduced below the normal to the extent shown by a pulse of 63, what must be the reduction in the central artery of the retina if we take as a standard Foster's figures just given? Furthermore, the axial stream in which the red cells travel is much quicker than the peripheral stream of plasma next the vessel wall. Here is certainly a condition favoring the separation of fibrin from the plasma, and the formation of Gutschy's primary fibrin membrane.

The next factor in thrombosis is alteration in the vessel wall. The patient has nephritis; it might, therefore, be said that she has endarteritis, arteriosclerosis, etc., but it is not likely, however, much as it would simplify things, if she had. Some change in the bloodvessel wall is very desirable for the purposes of this paper. This want is to be supplied by the bifurcation of the vessel. The point of bifurcation of the central artery of the retina—that point projecting in midstream, as it were—must necessarily stand more opposed to the onward flow of blood than the unobstructed wall. Such a mechanical arrangement causes a sudden halting of the stream with consequent embarrassment of some of the elements. Under these circumstances, and with an abnormally slowed current, the abovementioned changes of separation might well take place. This might also be favored by some individual peculiarity in the angle and form of bifurcation. This case shows peculiarities in the vessels of the

[1] Guy's Hospital Reports, series 2, vol. vii. pt. i.

[2] Foster's Physiology.

fundus, and it is not unreasonable to think that the vessels are also peculiar farther back. In support of this explanation is the experiment of Wharton Jones.

Changes in the blood itself have not been found. Two analyses were made by Dr. George P. Mueller, the second including an estimation of the fibrin. The first count gave: hæmoglobin, 100 per cent.; red cells, 4,650,000; white cells, 7650. Second count: hæmoglobin, 80 per cent.; red cells, 4,430,000; white cells, 5800. No increase in fibrin. Differential, normal.

This was somewhat of a disappointment as a functional heart murmur, which this undoubtedly was, is not usual with normal blood. My brother, Dr. Harvey Shoemaker, suggested that the blood quantity of the patient might be reduced as a whole. Cabot is authority for the existence of this condition. He has found it in typhoid fever, and attributes it to a concentration of the blood. There is no concentration of blood in this case, unless such concentration is offset by anæmia, for there is no increase of corpuscular elements, the ratio remaining unchanged.

Clinically the case suggests the following points: From the changes observed in the fundus I would locate the obstruction laterally in the central artery near or at the bifurcation and passing into the lower branch. If the lower arterial system alone were involved, there should be no changes in the upper vessels other than those brought about by doing extra duty or carrying more blood. But they were changed in size, contour, and light streak. An embolus to produce this condition would have to be of that rare variety in which the plug straddles the bifurcation. That the macular region was not more affected is attributed to the peculiar arrangement of the vessels described above. The more normal condition of the vessels at the periphery, and the subsequent return of some of them to their normal calibre are changes described in many of the reported cases of obstruction, and in the absence of any opportunity for collateral circulation in this locality have been thought to be due to backward flow from loss of *vis a tergo*. The keratitis and vitreous opacities are inflammatory, natural results of this condition. The white area so characteristic in these cases, is pathologically infarction, and not œdema, as invariably called. Secondary œdema does occur, but I am told reaches only to the edge of the infarcted area. The process is one of starvation.

Treatment. For the general treatment of cases of retinal artery obstruction, it is *important* to determine, if possible, whether or not the obstruction is thrombosis. Against embolism we are helpless, and the other eye will suffer or not, as fate ordains. But if the conditions contributory to thrombosis, as above outlined, can be established, they should be treated until they disappear.

Local treatment to be of any service must be immediate, and that these cases are sometimes seen early is shown by one of embolism

which Dr. de Schweinitz had under observation twenty minutes after the attack.

Now, as to the immediate treatment of arterial obstruction in the eye, whether from embolism or from thrombosis, I am convinced that pressure massage, which has been strongly advised by most writers, is irrational and should not be practised. Pressure on the eyeball stops what flow of blood still exists, and produces the most favorable conditions for further agglutination and accretion. It tends to fortify the obstruction. Surely the indication is to increase the force of the circulation without causing vasoconstriction or to increase the heart action and dilate the peripheral circulation. The drugs of one class will do this, viz., the *nitrites*, and best among these are nitroglycerin and nitrite of amyl. These drugs cause rapid heart action and a dilated peripheral circulation. Gifford has recommended nitrite of amyl. The use of any vasomotor constrictor, which will cause the artery to contract and thus hold tighter the thrombus or embolus, is clearly out of place.

But better than any drug, it seems to me, would be forced muscular exertion, such as running or climbing stairs. In this way the heart could be accelerated, and the peripheral circulation, if affected at all, dilated. Had my patient been enough frightened to run home, I believe she would have been benefited.

Another therapeutic procedure which might be indicated in some cases, and probably was in this case, is hypodermoclysis, or the injection of large quantities of fluid into the cellular tissue of the body for the purpose of rapid absorption into the circulation. Likewise the intravenous injection of saline solution should constitute a part of our resources.

The prognosis of these cases is well known, and I have nothing to add.

EMPYEMA OF FRONTAL SINUS, FOLLOWED BY EXTRADURAL ABSCESS AND ABSCESS OF FRONTAL LOBE; OPERATION AND DEATH FROM HYPOSTATIC CONGESTION OF THE LUNGS.

By Paul S. Mertins, M.D.,
MONTGOMERY, ALA.

Abscess of the brain resulting from empyema of the frontal sinus is a sufficiently rare condition to demand the report of cases. The case which I here present is that of Mr. W. D. L., a boilermaker, aged about forty years, who came to the office of Dr. M. L. Wood, September 8, 1903. For the past six months or more he has suffered from violent headaches, which have steadily increased in severity.

Within the last three days a swelling, the size of a goose-egg, has appeared in the region of the glabella. It was white, fluctuating, and very tender, and a harder rim, consisting probably of thickened periosteum, could be felt around its margin. On inquiry, a history of syphilis sixteen years ago was obtained. Two years ago he received a blow from a hammer on the top of his head, from which he was unconscious for several days.

The abscess was incised by Dr. Wood, and about one ounce of foul, dark-colored pus evacuated. The patient experienced complete and immediate relief of pain. He was instructed to go home, make hot applications to his head, and to return on the next day. On the third day the pain returned, and the patient noticed that when he held his head forward the flow of pus increased, and the pain became less. During the night of September 13th the pain grew more severe, the patient vomited several times, and had three convulsions. He was seen by Dr. Baker, who administered chloroform and morphine.

I saw Mr. L. on the following morning in company with Dr. Wood. He was in bed and seemed to be suffering greatly. His cerebration was slow, but relevant. No paralytic phenomena were observed. His pupils were small, equal in size, and reacted well. The eye movements were good in all directions. His breath was very foul, and the tongue, which was heavily coated, was protruded slowly in the centre line. His hand-grasp was strong, alike on both sides. His patellar reflexes were lively. No rigors have been noted. The ears were normal. The anterior end of the middle turbinate was greatly swollen. Temperature, 97.5° F.; pulse 78; respiration 20. His intimate friends stated that he has been considered stupid for a year or more, but his employer considered him an excellent workman.

On probing the wound necrosed bone was found, and in several places the probe seemed to enter the cranial cavity. A diagnosis of extradural abscess was made, and the patient was admitted to St. Margaret's Hospital for operation.

Operation September 14, 1903, at 3.30 P.M., under chloroform narcosis, Drs. Wood, Baker, and Pollard assisting. I performed the following operation: A three-inch incision was made in the integument of the forehead, through the seat of the abscess. The pericranium, which had been dissected from the bone by the abscess, was held back by retractors, and an area of necrosed bone, the size of a silver dollar, was exposed. It was of dark-brown color, and presented the appearance of a pepper-box top, from the numerous fistulæ through which pus oozed at each respiration. A half-inch trephine was applied to the centre of the necrosed area and a button removed. An extradural abscess, containing about one ounce of pus, was found. The trephine opening was enlarged with rongeur forceps to the size of a dollar. The dura was found adherent to the frontal

bone all around, and formed the bed of the abscess. Removing the necrosed bone opened the left frontal sinus, and about one-half ounce of pus was found in it. The right frontal sinus on being opened was found to be healthy. The wound having been irrigated with a boracic-acid solution, the dura was examined. It appeared to be very thick, was of a dirty yellowish color, and pulsated only on the left side. No fistulæ could be found. A hollow needle was introduced on both sides, with negative result on the left side, but with the finding of four or five drops of pus on the right side as the needle was withdrawn. The needle was repeatedly reintroduced on the right side, but pus could not again be found. The wound was irrigated and an iodoform gauze dressing applied. The patient was sent to the ward at 4.45 P.M. in good condition. One-half grain of morphine was administered. During the night he became delirious, tore off the dressings, and was kept in bed by an attendant.

September 15th. The patient's general condition was good; his mind, though much clearer than before the operation, was not entirely clear. He was in a nervous condition, and picked at the dressing constantly. The wound was dressed. The right side of the brain did not pulsate. The patient complained of no pain. Iodide of potash, 10 grains thrice daily, to be increased to 30 grains, was ordered, in view of the history of syphilis. Bromide of potash, 20 grains every four hours, for nervousness.

The wound was dressed daily. His bowels were obstinately constipated, and cathartics were necessary to obtain a movement. His urine was frequently passed involuntarily. This condition of irritability and semistupor continued. On September 23d a transient paresis of the right internal rectus was noted, and examination of the eye-grounds showed an optic neuritis on the right side. On September 24th, as the patient seemed to be in a more than usually stupid condition, and was unable to answer questions, I decided to aspirate the right frontal lobe again.

Second Operation. Drs. Wood and Baker were present. No anæsthetic was used. On introducing the aspirating-needle into the right frontal lobe at a depth of three-quarters of an inch, it was felt to enter a cavity and pus flowed into the aspirator. A small pair of scissors was entered by the side of the needle and the blades separated. About one and a half ounces of creamy pus and yellowish lump of broken-down brain tissue were evacuated. The cavity was gently curetted, and an iodoform gauze drain inserted. The patient's condition showed an immediate improvement. His mind became much clearer, and for the first time he spoke without a question being asked. His pulse rose from 78 to 100 beats per minute.

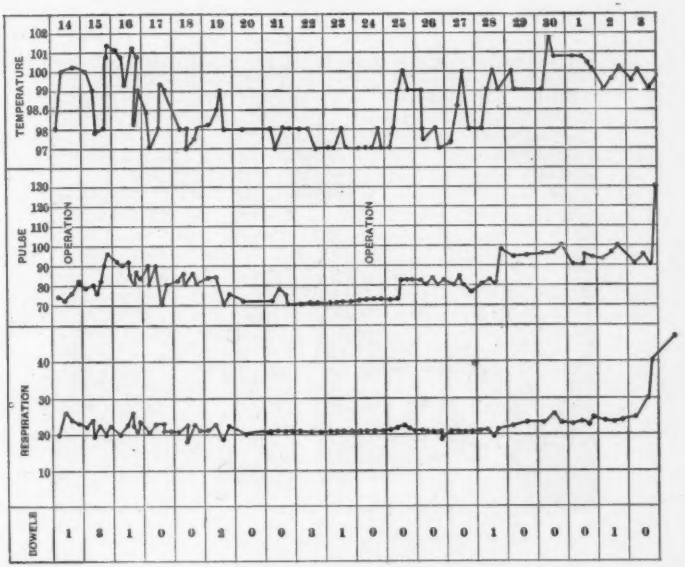
The accompanying chart gives the patient's pulse, respiration, and temperature while in the hospital.

The patient's condition continued to improve slowly. The abscess

cavity grew smaller and the discharge less. Granulations began to cover over the exposed dura. His appetite continued good and his mind clear. The wound was dressed daily.

On the evening of September 30th I found a marked change in the patient's condition. His mind was less bright and his answers were much slower. His temperature was 102° F., pulse 98, and respiration 24. The wound was in good condition and draining freely. Examination of the chest showed a hypostatic congestion of the inferior lobe of the right lung; and the nurse informed me that during the afternoon the patient had coughed up several mouthfuls of blood. Strychnine $\frac{1}{30}$ grain and brandy $\frac{1}{2}$ ounce every four

FIG. 1.



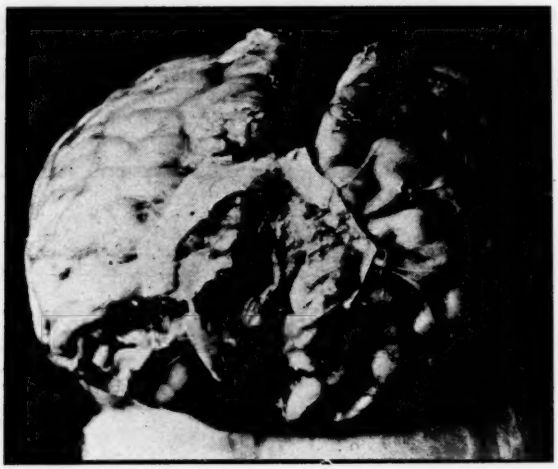
hours was ordered, and directions were given to change the patient's position often. On October 3d the left lung became involved, and the patient's condition much worse. His urine and feces were passed involuntarily, and his pulse and temperature rose. His mind continued clear.

On the morning of October 4th he had a hemorrhage of several ounces. Morphine $\frac{1}{4}$ grain was given, and an ice-bag was applied to the chest. He was unable to take his nourishment, and died on the morning of October 5th, twenty-one days after the operation, from exhaustion.

Autopsy fourteen hours after death. Drs. Wood, Hudson, Pitts, Billings, and William Thigpen were present. On removing the

scalp a depressed fracture, the size of a hammer-head, and about one-half inch deep, was found on the left parietal bone, near the sagittal suture. An opening the size of a match-head was found at the bottom of this depression. The bone was healthy, and this was probably the result of the blow received two years ago, from which he was unconscious for several days. On removing the calvarium the dura was found to be adherent around the original trephine opening, both to the bone and to the brain. It was also adherent to the bone at the point of the depressed fracture. The membranes appeared normal, and no increased amount of cerebro-spinal fluid was noticed. The brain appeared normal, except at the point of operation, where an opening, 1 cm. in diameter, was

FIG. 2.



Photograph of brain, showing opening of abscess and adherent dura.

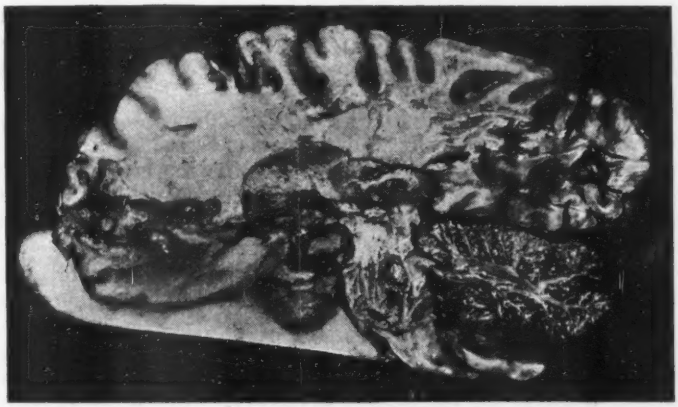
found leading into an abscess cavity. The longitudinal sinus was found normal. The brain was placed in a solution of formalin to harden. On opening the thorax the heart was found normal. Both inferior lobes of the lungs were found to be in a condition of hypostatic congestion, and on section of the right lung a cavity the size of a walnut, filled with clotted blood, was found. Old adhesions were found on the left side, between the pleura of the lung and diaphragm. The abdominal cavity was not opened.

The photographs of the hardened brain show the location and size of the abscess. In the photograph of the entire brain the dura has been left adherent to the brain about the abscess opening, showing that the abscess was well walled off. The opening into

the abscess is seen as a dark spot on the right side. The small rupture in the brain was made in removing the skull-cap. In the sagittal section the depth of the abscess, one and one-half inches, is seen. In this section the abscess was found to be well walled off by a thick lining membrane. The brain tissue about the abscess was in a nearly normal condition.

The dark area below the abscess is an extravasation of blood.

FIG. 3.



Anteroposterior section of brain, showing depth of abscess cavity, a part of lining membrane, and hemorrhagic focus below abscess.

REMARKS. From the condition of the brain at autopsy, I think we have every reason to believe that this patient would have recovered from his abscess. The pulmonary complications were, without doubt, the cause of death. The abscess was the direct result of the empyema of the frontal sinus. The posterior wall of the sinus was necrosed and a fistulous tract was found from the sinus to the extradural abscess. This case is similar to that of Roth[1] in many respects; an external abscess was found, an extradural abscess and abscess of the left frontal lobe. His patient died. Macewen[2] reports a case of abscess of the frontal lobe with recovery. This case was, however, of traumatic origin. Professor G. Killian[3] discusses three other cases of intracranial complications following empyema of the frontal sinus, namely, those of Carver,[4] L. Müller,[5] and E. Fraenkel.[6]

[1] Wiener klinische Wochenschrift, 1899, No. 14, p. 383.
[2] Pyogenic Diseases of the Brain and Spinal Cord.
[3] Archives of Otology, August and October, 1901.
[4] British Medical Journal, June 16, 1883.
[5] Wiener klinische Wochenschrift, 1895, p. 194.
[6] Virchow's Archiv, vol. cxliii. p. 80.

CHONDRODYSTROPHIA FŒTALIS.*

By P. W. Nathan, M.D.,
of New York.

The majority of chondrodystrophic individuals are either born prematurely or born dead at term. The affection is, therefore, a very serious fetal disease, with a high mortality. Those infants which are born alive are usually very weak, and for some time life is precarious; should they, however, survive this critical period, they seem to grow stronger, and later they are *no* weaker than normal infants of the same age.

The nature of the affection thus accounts for the fact that up to the present time practically all the reports of cases have simply contained post-mortem findings. The earlier observers contented themselves with a description of the external characteristics; and these they found so closely analogous to those found in rachitic infants that they found no hesitation in classing the two conditions together. Thus the disease became known as an antenatal prototype of rachitis, being sometimes called congenital rachitis, sometimes fetal rachitis.

The earliest published case dates back as far as 1791, when Sömmering[1] reported his post-mortem findings of a case of fetal abnormality, which he did not attempt to classify. From his description, which is fairly accurate, there can be no doubt as to the nature of the condition. The bones are said to present the characteristic rachitic abnormalities; the fœtus is obese; the extremities are much too short, and much bent and deformed. In 1836 Busch[2] gave a very accurate description of a case, which he called congenital rachitis. He notes all the salient features which characterize these cases, viz., very large head; short, deformed extremities, with hard skeleton, large epiphyses, so-called rachitic rosary, rachitic pelvis, and general obesity. Following him numerous writers gave more or less accurate descriptions of cases which, in the light of our present knowledge, may be considered cases of chondrodystrophia fœtalis.

The majority of these writers, however, drew their conclusions as to the nature of the abnormality from the more or less cursory examination of a single case; and it was not possible, until the publication of the more extensive and careful observations of H. Mueller[3] (1860), to formulate a distinct and coherent idea of this singular affection. H. Mueller's researches, which are remarkable for their accuracy and insight, may be said to have formed the basis for all future investigation. He showed decisively that chondrodystrophia is a disease of the primordial bone cartilage; that it has nothing in

* Read before the Orthopedic Section of the New York Academy of Medicine, Oct. 16, 1903.

common with rachitis, and that the inhibition of the growth of the long bones, which is the most prominent characteristic of the condition, is due to a disturbance in the row formation of the proliferating cartilage cells. The examples which he first examined occurred in calves, but he re-examined the cases previously published by Virchow as congenital rachitis and congenital cretinism, and found that in man the pathological phenomena are identical.

Some time afterward (1873) Urtel[4] carefully examined a still-born child macroscopically and microscopically, and his findings were identical with those of Mueller in the principal features; he hesitates, however, to place his case in the same category, because they differ in some particulars. Later investigation has proved his hesitation unwarranted.

The further development of our knowledge of chondrodystrophia fœtalis we owe to Eberth,[5] Schidlowsky,[6] Kirchberg,[7] Marchand,[8] but above all to Kaufmann,[9] who, having special opportunities for investigation (he had thirteen cases), was enabled to clear up many points in the pathology.

External Appearance. The appearance of a chondrodystrophic fœtus is characteristic. The head is very large and appears still larger in contrast with deficient length of the fœtus as a whole. Both upper and lower extremities are too short. The arms do not reach the waist-line, and the lower extremities are so short that decentralization of the body is produced. Thus, the midpoint between the crown of the head and the soles is not, as it should be in normal infants, at the navel, but above it; in many cases as high as the xiphoid cartilage. The extremities, moreover, are bent and deformed, and occasionally fractured. All the epiphyses appear more or less enlarged, and those of the ribs produce the so-called rachitic rosary. The skin and subdermal tissues are hypertrophied, causing an exaggeration of the natural skin-folds; the abdomen is prominent, and the fœtus as a whole appears very obese. There is frequently epicanthus; the lips, eyelids, and tongue are thickened, and the latter protrudes from the mouth.

The anomalies of the skeleton give the fœtus that peculiar appearance which has long been known to be characteristic of rachitis, and which has led so many observers into the error of associating these two conditions. But aside from the pathological differences, which will be spoken of later, the peculiarity of the head and face in chondrodystrophia fœtalis should lead one to suspect that, similar as are the other external phenomena, these at least are peculiar to another affection.

As has been pointed out, the head is abnormally large; indeed, it is so large that its circumference equals the length of the body, and in many cases exceeds it. The distinguishing characteristic, however, is the decided prognathus, with marked retraction of the nose, and, in some cases, flattening of the whole nasal region. The latter

abnormalities very much resemble those of infantile myxœdema, and where, as is usually the case, they are associated with thick lips, protruding hypertrophied tongue, epicanthus, and prominent abdomen, the resemblance to the congenital cretin is so close that without a microscopic examination of the bones, or a clinical history, the two conditions cannot be differentiated.

Pathological Anatomy. Before proceeding to the discussion of the pathological changes at the base of the skull, a few words as to its anatomy and development are necessary.

Upon the development of the base of the skull depend the peculiarities in the shape of the head and the physiognomy. Most important in this respect is that portion of the base of the skull which Virchow designated the os tribasilaris, and Hyrtle the fundamental bone. This bone is composed of the basilar process of the occipital bone, the os basilaris posterius, and the two portions of the body of the fetal sphenoid, the os basil. ant. and os basil. med. These three parts of the compound bony os tribasilare are, in fetal life, separated by synchondroses, the synchondrosis intersphenoidalis and the synchondrosis spheno-occipitalis, which at birth are only partially ossified. Normally the synchondrosis intersphenoidalis is ossified at birth or soon thereafter; the synchondrosis spheno-occipitalis, however, remains patent until at least the thirteenth year, and complete synostosis occurs between the eighteenth and twentieth years. The growth of the base of the skull depends upon the persistence of these synchondroses; synostosis or even a disturbance in their development therefore produces a shortening of the base of the skull. As deficiency in the length of the base of the skull always causes prognathus, the relation of the above-mentioned synchondrosis to the prognathus is evident. In the case of so-called congenital cretinism, which Virchow[10] used to demonstrate this fact, there was complete synostosis of the synchondroses os tribasilare, but he did not claim that synostosis was necessarily present in every case of prognathus. On the contrary, he laid particular stress upon the fact that not alone synostosis, but any deficiency in the length of the base of the skull would cause this anomaly. The writers following him, however, assumed that synostosis was the cause of prognathus in all cases; and this opinion was generally held, though the observations of Klebs,[11] His,[12] Marchand and Paltauf[13] were opposed to such an assumption. In his examination of thirteen cases of chondrodystrophia Kaufmann was enabled to settle this question definitely; he found that not alone premature synostosis of the os tribasilare, but *any* inhibition of the growth of the os tribasilare or inhibition of the growth of any of the bones at the base of the skull causes prognathus. He found that synostosis of the os tribasilare was present in many cases of chondrodystrophia fœtalis, probably in the majority of them, but in a certain number the synchondroses are patent. Moreover, Kaufmann showed, by careful measurements of all the

bones at the base of the skull, that though the os tribasilare is a very important factor in its growth and development, it is not the only factor; for in some of his cases there was retraction of the root of the nose, though the os tribasilare was of the normal length. Even in those cases in which the os tribasilare is shortened or synostosed, it must not be assumed that this is the only part which is instrumental in causing the prognathus; not infrequently the bones anterior, the ethmoid, and nasal are also involved, either taking part in the shortening or, as occasionally happens, being entirely responsible for it (Kaufmann's Case XI.).

Another peculiarity of the base of the chondrodystrophic skull, first pointed out by Virchow, is a reduction in the angle formed at the junction of the basilar process of the occipital bone and the body of the sphenoid. Virchow called this condition kyphosis of the saddle angle.*

We must, therefore, conclude that the conditions which are active in causing the peculiar physiognomy in chondrodystrophia fœtalis vary within rather wide limits. They may be enumerated as follows: 1. Most frequent is premature synostosis, and consequently inhibition of the growth of the os tribasilare, with or without shortening of the bones anterior. 2. Shortening of the os tribasilare, patent synchondroses, varying degree of shortening of the bones anterior. 3. Decided shortening of the ethmoid and nasal bones, with slight or no shortening of the os tribasilare, and patent synchondroses. With these is associated a change in the saddle angle (kyphosis) of varying extent.

The bones of the skeleton present a variety of changes. They are always shortened and apparently thickened. In only a small percentage of cases, however, are the bones really thickened; as a rule, the apparent increase in thickness is due to the shortening, which changes the ratio between the length and thickness. The same is true of the epiphyses, which always appear larger than normal, though they are really enlarged in only a certain percentage of cases. In some cases, however, the epiphyses are enormously enlarged.

Sections of the long bones show that the pathological change occurs primarily in the growing cartilage. This portion of the bone, though it shows a variety of changes, is invariably affected in every case. The vascularity is always increased, but its size and consistency vary in different instances. According to the latter, Kaufmann distinguishes three distinct types: First, the epiphysis is not enlarged and the consistency is normal; second, it is absolutely enlarged, and the consistency may or may not be changed; third, the cartilage is softened.

The microscopic examination of the bones shows changes in the growing cartilage which correspond to the gross changes just enu-

* Normally the saddle angle increases from the third fetal month until birth, when it is 155°; thence it diminishes to puberty.

merated. There is, however, one change which is constant and characteristic. This is the more or less complete inhibition of the normal row formation of the proliferating cartilage cells in the preparatory stage of ossification. The limitation of row formation is not, however, the same in all cases; though it is never absolute, in some cases it is almost so, and there is only a suggestion of row building in isolated areas of the ossifying zone. On the other hand, there are others which may, with propriety, be called mild cases, in which the row formation occurs, though the rows are stunted and rudimentary, inconstant, and irregular. Between these two extremes all gradations occur.

In the class of cases referred to as type one, which shows no increase, but rather a diminution in the size of the epiphyseal cartilages, besides the limitation in the row formation, there is also an inhibition of the proliferation of the cartilage cells. For this reason Kaufmann designates this type of cases chondrodystrophia fœtalis hypoplastica. In contrast to these is type two; here, though the row formation is rudimentary, the cartilage cells, instead of showing defective proliferation, are, on the contrary, enormously increased in numbers, and very closely packed together, causing the characteristic enlargement of the epiphyseal cartilage. This type Kaufmann designates chondrodystrophia fœtalis hyperplastica. The intercellular substance of the cartilage other than increased vascularity shows no change in the two types of the disease just described; in the third type, however, this is also abnormal. Here the cartilage has softened, in the severer cases quite extensively so, and the epiphyses appear as more or less completely gelatinous and very vascular masses, with variable dimensions. The intercellular substance is distended and forms an irregular network, in which cells of varying size are irregularly distributed. These cases Kaufmann designates chondrodystrophia fœtalis malica.

Thus, according to Kaufmann, we have three distinct types of chondrodystrophia fœtalis, viz., chondrodystrophia fœtalis hypoplastica, chondrodystrophia fœtalis hyperplastica, and chondrodystrophia fœtalis malica. Between these three types the rudimentary row formation is the connecting link, for it occurs in all of them, and is, therefore, the most characteristic and uniform change. Moreover, it must not be supposed that the three types occur perfectly distinct as individual cases; all three types may be found in the same individual in the various epiphyses, though one type usually predominates in a given case.

These pathohistological changes occur in all the bones subject to enchondral ossification, and they readily account for the dwarfism of not alone the long bones of the skeleton, but also for the shortening of the base of the skull and the resultant cretin physiognomy. The variation in the intensity of the process and its modifications, evidently, cause the variation in the conditions found in the latter

region. Thus, the prognathus may be due to the hypoplastic, the hyperplastic, or the malic process; any one of which may affect the cartilaginous skull in its entirety or one or more of the primordial cartilages more than others. With the cessation of the row formation, further bone development becomes impossible, and, as a result, ossification takes place, which may or may not be complete, according to the severity of the pathological process. Hence we find all gradations, from complete synostosis of the primordial skull vertebræ (os tribasilare) to only slight shortening, with patent synchondroses. In the malic form of the disease the affected primordial cartilages are soft, the ossification centres are rudimentary or even absent, and in the severer cases growth ceases entirely.

Synostosis of the synchondroses os tribasilare is, therefore, not, as the earlier writers assumed, necessarily present in all cases of chondrodystrophia fœtalis. Nor is the os tribasilare shortened in every case; so that the absence of either or both of these conditions does not decide the doubt, if any exists, that we have chondrodystrophia fœtalis before us in a given instance. All the bones at the base of the skull, which develop from cartilage, must be measured, and should the diagnosis still remain doubtful, it can always be cleared up by the microscope.

Besides the disturbance in the proliferation cartilage cells, there are still other peculiarities of the chondrodystrophic skeleton revealed by the microscope. It is found that the deposition of the calcium salts, no matter how great the abnormalities in the cartilage, goes on in a perfectly normal manner; the line of calcification is always found to be fairly regular, and the formation of ostoid tissue and its ossification is typical. Still more remarkable, considering the gravity of the pathological process in the cartilage, is the fact that periosteal bone formation goes on in a perfectly normal manner. Not alone this, but all the bones or parts of them which are formed and ossified very early in fetal life, or directly from connective tissue, pursue their normal course of development and show no abnormality. Thus the clavicle was found to be normal in length and other respects in all the cases reported; so also the bones of the cranial vault and all other bones similarly developed. In the long bones the normal development and ossification of the periosteal bone stands out in sharp contrast to the short and defective enchondrium, and the change in the ratio of the row gives rise to the appearance of thickening, to which attention has been called.

A very remarkable and interesting phenomenon which occurs in a great many and at some point in the skeleton in all cases of chondrodystrophia is what the Germans call the periosteal lamella. This very peculiar formation, which was first described by Urtel as it occurred in a human fœtus, later by Eberth in the calf, and subsequently by nearly all authors on this subject, consists of a layer of connective tissue emanating from the periosteum, from which it

pushes its way between the epiphysis and diaphysis toward the axis of the bone. Thus the epiphysis and diaphysis are separated more or less completely from each other. The periosteal lamella, which for reasons which will appear later I shall call the periosteal inclusion, varies in extent in the different cases and in the various parts of the skeleton in the same case. In the majority of instances it begins in the periphery as a distinct band, but gradually diminishes in breadth toward the axis of the bone, where it disappears. It is often apparent macroscopically, forming a distinct wall at the epiphyseal line, but it varies to a considerable extent, and not infrequently is only visible with the aid of the microscope. The breadth and the depth from the periphery usually correspond, so that when it is narrow it only invades the bones for a short distance, leaving a considerable portion of the axis free.

Microscopically, it can be seen that the cartilage cells adjacent to the periosteum inclusion run parallel with it, and assume a spindle form. The intercellular substance of the cartilage is fibrillated, and thus the transition between the inclusion and the cartilage is very gradual, at times almost imperceptible. On the diaphyseal side the conditions are liable to some variation. In some instances the inclusion undergoes ossification, with the formation of true bone, in a manner exactly similar to that which occurs under the normal periosteum (Urtel,[4] Hoess,[14] Eberth,[5] Bode,[15] Sturp,[16] and others). In others, as in Kaufmann's Case II., the inclusion is surrounded by cartilage on both sides.

The relatively greater production of periosteum, as compared with the enchondral growth, is considered by all authors as the underlying cause of the periosteal inclusion. The manner of its production, however, is subject to some difference of opinion. Some authors (Urtel, Hoess) consider it due to an invasion of the cartilage by a periosteal process, due to an active local proliferation of the periosteum; and Kaufmann considers his Case II., in which the inclusion is surrounded by cartilage on both sides, as demonstrative of such a manner of production. It is difficult, however, to understand why the periosteum should proliferate excessively in a given locality without assignable cause. Eberth's explanation seems more plausible; he believes that the inclusion is due to the overgrowth of the epiphysis beyond the peripheral diaphyseal line, causing an involution of the periosteum, which subsequently proliferates. Kirchberg and Marchand also attribute the cause to an involution of the periosteum, but they consider this involution due to a continued growth of the periosteum, without a corresponding increase in the length of the bone.

Personally, I believe that all these conditions, and not a single one alone, are, to some extent, responsible for the formation. I imagine the process of development to be somewhat as follows: The epiphysis enlarges until it grows beyond the peripheral diaphyseal

line, thus causing an involution of the periosteum at the point where the epiphysis and diaphysis join. Subsequently the diaphysis grows in thickness, but not in length, so that the fold of periosteum, instead of being eradicated (as it would be if the growth in length and thickness were in the normal ratio), becomes more pronounced, and is included between the adjacent surface of the epiphysis and diaphysis. The inclusion continues to act as periosteum; it therefore proliferates, forms ostoid tissue and true bone.

The periosteal inclusion, by its encroachment upon the epiphyseal line, necessarily precludes growth in length; and Kaufmann believes that this cessation of growth is analogous to that experimentally induced by injury or removal of the intermediate epiphyseal cartilage. But it must not be hastily decided that the cessation of growth is always absolute; in some cases the inclusion is very rudimentary, leaving a considerable portion of the axis of the bone free, and here the row formation, though defective, may still go on. It is only in those cases in which the periosteal inclusion is very extensive and undergoes ossification, thus causing synostosis of the epiphyseal synchondroses, that growth is definitely concluded. (Examples of such a condition occur in the os tribasilare and also, but less frequently, in the long bones.) Naturally, the earlier in fetal life the disease begins the more rudimentary is the row formation, the more complete the periosteal inclusion, and the more limited the growth of the long bones.

Thus, from an anatomical point of view, chondrodystrophia fœtalis is a well-defined morbid condition, and if we bear in mind its salient features, there can be no difficulty in differentiating it from other affections. The characteristic signs are defective growth of the enchondral skeleton, including the base of the skull and the pelvis, which, upon microscopic examination, is found to be due to the rudimentary row formation of the proliferating cartilage cells and the periosteal inclusion. In contrast to this is the normal ossification and the normal development of the periosteal and membranous bone. With postnatal rachitis it has absolutely nothing in common, except the apparent enlargement of the epiphyses, the prominent abdomen, and the occasional bowing of the legs; the latter is due to entirely different causes, which cannot be discussed here. Osteogenesis imperfecta, with which it has been confounded, differs from it in all the essential details. Here the salient pathological condition is a deficiency of ostoid tissue and defective ossification; the bones are of normal length, and the skull and all the other morbid changes of chondrodystrophia fœtalis are absent. Osteoporosis and osteosclerosis may both occur as complications of chondrodystrophia, but when present they are always secondary to the changes already described, and not pathognomonic.

Before closing our review of the pathology of this very interesting condition, though time presses, I cannot omit a few words as to the

Fig. 4.

Fig. 3.

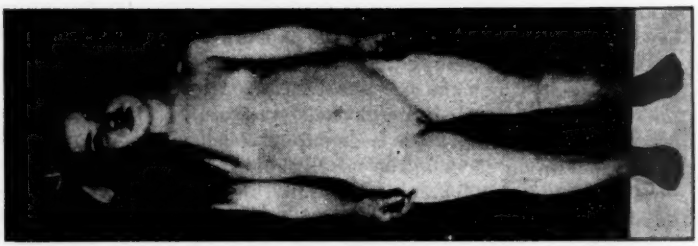


Fig. 2.

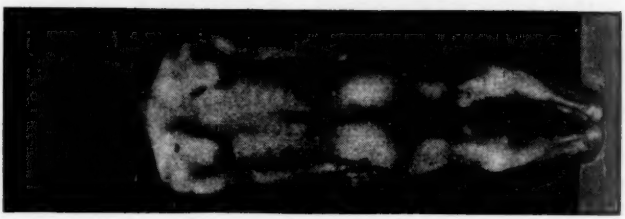
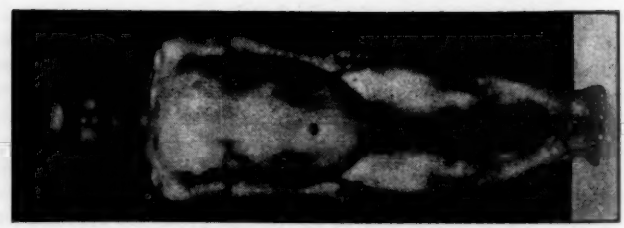


Fig. 1.



pathogenesis. Mueller, Eberth, and a large number of authors consider the nature of this anomaly analogous to that of congenital cretinism. However, though the skin and skull lesions lend some support to this view, clinical experience and the pathological anatomy teach us that the two diseases have nothing else in common. I think the changes in the skeleton and in the subdermal tissues point very distinctly to a constitutional anomaly, which, though not exactly analogous to that of congenital cretinism, nevertheless acts upon fetal organism in a similar manner; that is, by disturbing the metabolism in some unknown way.

Clinical Aspect of Chondrodystrophia Fœtalis. As has been said, the majority of infants with chondrodystrophia is born dead. But the disease is not nearly so uncommon as some authors would have us believe; and to judge by the number of living examples to be found in the literature, and my own experience, it is not necessarily fatal. Quite a number of isolated cases have been reported, and recently Kassowitz[17] has described seven cases which came under his own observation. I have had the opportunity to examine eight cases, a number of which I still have under observation. One I have re-examined after an interval of several years (Case IV.); he was shown by Dr. C. Hermann, in the Pediatric Section of the Academy some time since. I show you his photograph, with that of Case V. Moreover, I have seen a number of adult cases walking about, and though I had no opportunity to examine them more closely, their appearance was so characteristic that I do not hesitate to classify them. All my cases were seen within the last three years, and it is for this reason that I consider chondrodystrophia not nearly so uncommon as has been supposed; and I believe this statement will be borne out by general experience when the knowledge of this disease becomes more universal.

The general appearance of a chondrodystrophic infant differs very slightly from that of a fœtus with the same disease. They are dwarfs, with a large head, and very short, often bowed, extremities. In infants the abdomen is very prominent, as are the epiphyses, and there is obesity, but in the older cases these symptoms, though present, are not nearly so distinct. The head is large; in the younger individuals its circumference equals the length of the body in measurement, and there is a decided prognathus, which is accented by very marked retraction of the root of the nose, or flattening of the whole nasal region. The hair on the head is abundant, fine and soft, in my cases never coarse or brittle.

The lower extremities are always too short, being entirely out of proportion to the length of the trunk. This causes a decentralization of the body and tends to give these individuals a very characteristic, at times ludicrous, appearance, and very readily distinguishes them from other dwarfs; for in cretinism, or in the so-called idiopathic dwarfism, the extremities and the trunk are both shortened and are

not out of proportion. The disproportion between the trunk and extremities in chondrodystrophia is readily demonstrated by measuring the height of the individual, first standing, then sitting. Measured in this way, my cases showed this peculiarity very distinctly:

	Height standing.	Height sitting.
Case I.	21½ inches.	15½ inches.
" II.	28¾ "	18⅛ "
" III.	23 "	14¾ "
" IV.	45 "	29⅛ "
" V.	47⅞ "	30 "

The decentralization is also very well demonstrated by comparing the distance between the crown of the head and the umbilicus to that between the umbilicus and the sole of the foot. In the normal newborn infant these are the same, but as the child grows the distance between the umbilicus and the soles increases much more rapidly than the other, and exceeds it more and more as the individual grows older. In chondrodystrophia the midpoint of the body is not at the umbilicus at birth, but above it, sometimes as high up as the xiphoid cartilage, and this disproportion or decentralization of the body continues throughout life.

The upper extremities are also too short; they do not, as in the normal individual, reach to the hips. The fingers and toes are short, and, in fact, the conditions found in the living subject are exactly what the pathological anatomy would lead us to expect.

During early life these individuals are obese, and the natural skin folds are exaggerated, but as they grow older the obesity gradually disappears. In all the cases I have examined, and as far as I can tell from the reports of other cases, the skin is never harsh and scaly, and the development of the hair on the head and other parts of the body is perfectly normal.

The mental faculties are always intact; these children are not sluggish and somnolent, but bright, taking an intense interest in their surroundings and learning to talk as readily as other children. If the older individuals are backward in their studies, it is more because they are apt to be kept from school because of their small size and peculiar appearance than from lack of intelligence. They begin to walk late, as a rule, and those cases with complicating osteoporosis do not do so for a long time; but when they have learned to walk their gait is in no way peculiar or unsteady.

Like all infants with congenital abnormalities, they usually present some other congenital defects. The most frequent of these is inguinal hernia and a highly arched palate. In some of the postmortem findings dislocation of the hips is noted, but I have not been able to trace a direct causative relation between chondrodystrophia and the ordinary cases of congenital dislocation of the hip which we see in practice. Kassowitz attempts to bring them in connection, but I can hardly agree with him when he considers the fact that

patients with congenital dislocation of the hip are liable to other congenital malformations, such as epicanthus, highly arched palate, etc., as an indication of a connection between the two abnormalities. As I have pointed out, all individuals with one congenital malformation are very apt to have others. Moreover, I have carefully examined some twenty cases of congenital dislocation of the hip without being able to find any trace of chondrodystrophia. I must not, however, be understood to deny the possibility of the occurrence of dislocation of the hip in chondrodystrophia; I simply deny its causative relation to congenital dislocation of the hip in general.

Kassowitz also groups chondrodystrophia with mongolism and myxœdema. In practice there is hardly any danger of confounding these affections. The mongols are idiots, without any disproportion of the skeleton, and with a characteristic mongolian physiognomy, which is absolutely distinct from that of chondrodystrophia. Myxœdema is very readily distinguished from it; there is always mental defect; there are the skin and hair changes, and the disproportion between the extremities and the trunk is not present. That all three diseases have the abnormalities which are apt to appear in all congenitally abnormal individuals is certainly no reason for grouping them together, though Kassowitz very naïvely considers this a scientific classification. That this disease, like cretinism and some others, antenatal and postnatal, may be caused by a disturbance of the metabolism can, in the light of our present knowledge of the normal metabolism, be neither positively affirmed nor denied. In chondrodystrophia the thyroid gland and the organs other than the skeleton show no change perceptible to us, and we must confess that the pathogenesis of this, as well as of nearly all other diseases, is still unexplained.

Of the etiology we know nothing. In one case a chondrodystrophic mother is said to have given birth to an infant similarly affected, but in all others we have nothing upon which to base a surmise as to the cause of this disease. To judge by the cases reported, the female is somewhat predisposed, though my own cases are equally divided between the two sexes.

MEASUREMENTS.

(Cases VI., VII., and VIII. were not accurately measured.)

	Case I.	Case II.	Case III.	Case IV.	Case V.
Age	16 mos.	4½ yrs.	9 mos.	14 yrs.	14 yrs.
Sex	Male.	Female.	Male.	Male.	Female.
Height standing	24¼ in.	28½ in.	23 in.	45 in.	47¾ in.
" sitting	15½ "	18⅝ "	14¾ "	29½ "	30 "
Circumference of head	17½ "	20¾ "	17⅝ "	19⅞ "	
Length from crown to umbilicus	.....	14 "	12½ "	.....	21 "
" " umbilicus to sole	.....	14½ "	10½ "	.....	26 "
Ant. sup. spine to ankle	7¼ in.	13¾ "	9½ "	18½ in.	20¾ "
Femora	.....	6 "	9½ "	10¾ "	
Tibiæ	R. 3½ in.	R. 6¼ "	R. 14½ "		
"	L. 3¼ "				
Arms	3½ "	.....	.....	6½ "	
Forearms	3½ "	.....	.....	6½ "	

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LEUCONYCHIA STRIATA ARSENICALIS TRANSVERSUS.

WITH REPORT OF THREE CASES.

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Five years ago at the Cleveland City Hospital, while examining a woman suffering from a very severe arsenical neuritis, I was struck by the observance of a peculiar white transverse line occupying the middle of the outer third of the finger-nails of each hand.

Taking into consideration the fact that the nails grow more rapidly following arsenical poisoning, I was able to estimate that these white lines corresponded to the time when, with suicidal intent, she had taken a teaspoonful of "Rough on Rats," which is well known to contain a large quantity of arsenic. The white streaks were about one-sixteenth of an inch in width, quite regular, with fairly sharp margins, and occupying an identical position on each nail. They were slightly larger on some nails than upon others and a little wider in the centre than near the margins; extended from side to side, forming a crescentic band, with the convexity directed to the free margins of the nail, and presenting a curve identical with that of the lunula. The markings were less plainly seen upon the toe-nails. Her body was covered with branny exfoliating dermal scales; much of the hair had fallen, and the palms and soles showed some kera-

tosis. At that time I looked through the literature very carefully, but was unable to discover any reference whatever to such lines occurring in arsenical poisoning, and while I felt positive that in my case they were caused by the mineral, yet decided to wait for further confirmation of that opinion.

About twelve months following the observation of this case I was consulted by a man with an undoubted neuritis, who had been referred to me by Dr. F. W. McLean, of Elyria, and who gave the following history:

He had suffered a very violent attack of "stomach difficulty" about three months preceding his visit to me. He says the vomiting was so violent that the vomitus contained blood. He did not suffer any marked cramps in the legs or arms. Shortly after he began to grow weak in his legs, and at last was barely able to get about with two canes.

FIG. 1.

On examination I found he was ataxic, had a partial double foot-drop, absent knee-jerks, some loss of sensation, no pigmented spots or keratosis, no loss of sphincter control. In short, he had all the symptoms of a multiple neuritis. Inspection of his nails showed the characteristic transverse streaks as described, and as illustrated in this rather poor photograph (Fig. 1). It does not show the striation plainly. After talking with the patient some little time, during which he asked my opinion, I told him I thought he would probably recover from the neuritis, and that the neuritis was undoubtedly due to poisoning. At first he demurred, but after a little conversation told me that he believed he had been poisoned, but offered no explanation except that he was positive that it was arsenical poisoning. After urging upon him the necessity and the perfect safety of giving me his confidence, he confessed to having taken a large dose of white arsenic, but stated that it immediately produced vomiting, and ultimate recovery took place, save his nerve inflammation.

In May, 1899, Dr. George Gill, of North Ridgeville, Ohio, referred to me a patient giving the following history:

F. S., male, white, aged twenty-nine years; has a wife and two healthy children. The wife is healthy; one induced miscarriage seven years ago. Patient gives a history of good health in early childhood; in early manhood gonorrhœa, but no history of lues. I cannot learn that he has had any other sickness. He uses tobacco and drinks to excess. He states that one night about three months ago, on returning home from a debauch, he concealed a bottle of whiskey beside a hedge-row near his house. Becoming thirsty about 1 o'clock the next day he sought the bottle and took a large drink. In a short time he began to suffer extremely from pain in the stomach, vomited almost continuously, had cramps in the legs and arms, and became unconscious. His vomiting continued until 10 o'clock the following day. He remained in bed three days, and then got up, feeling very weak and still suffering from occasional attacks of vomiting and colicky pains in the abdomen. Six weeks later he began to feel tired, sore, and lame; the legs grew weak, the arms and hands felt heavy, weak, and numb. There was no loss of bladder power, but considerable diminution of sexual power. He unhesitatingly expressed to me the opinion that his uncle, with whom he had had trouble, had put poison in the whiskey.

Examination. Patient is a fair-sized man, walks with canes, gait ataxic; partial double foot-drop; station is not good, in fact, without his canes he is unable to stand with the eyes open. Both knee-jerks are absent, wrist-jerks and elbow-jerks are also absent. He is slightly anæsthetic throughout the lower limbs, which anæsthesia grows more marked as the extremities are approached. He is proportionately more analgesic than anæsthetic. The fingers are slightly anæsthetic; he is unable to button his clothing well or to handle small objects. There is no tremor. The hand-grasps are equal and weak, registering thirty-six. There are no scars or spots on the body, and in fact nothing else abnormal is noted, except a white, slightly crescentic transverse streak on each finger-nail; the convexity of the crescent is directed toward the free margins. These streaks were so strikingly like those of the related cases that I immediately informed him that his stomach attack was due to arsenical poisoning. It was at this time he told me about the whiskey, adding that he thought his uncle had poisoned him. Shortly after this, in answer to some inquiries regarding the case, I received a communication from Dr. Gill, who informed me that the man had made a confession, which was corroborated by his wife, that he had taken a quantity of "Rough on Rats," with suicidal intent.

The accompanying black and white drawing (Fig. 2) affords an exact representation of the condition of his nails, and, indeed, the appearance common to each of the three cases observed. There were no transverse ridges on the nails, nor furrows; the lines were, in longitudinal relation at about the point which we would expect them to occupy from the outward growth of the nail since the poison-

ing. His toe-nails also showed faint markings, but no keratosis was present on the palms or soles.

I was about to publish these cases when I noticed the report of a case of arsenical neuritis by Dr. Florence Sabin, in the May number of the *Johns Hopkins Hospital Bulletin*, 1901, in which a white line running transversely across each finger-nail was referred to. In answer to a letter to Dr. Sabin, I received the following reply:

"Your note in regard to the white lines in the nails in cases of arsenical poisoning has interested me greatly. I do not know of any references in the literature, and Dr. Osler says that he does not. Dr. Osler expressed himself as anxious to see the photographs of your cases."

FIG. 2.

Since the observation of a large number of cases of arsenical neuritis reported as occurring in beer-drinkers throughout England, and especially about Manchester, I have had considerable correspondence in reference to the condition of the nails with the English physicians observing those cases.

In April, 1901, Dr. Nathan Raw, of Manchester, wrote me that he had observed changes in the nails, particularly the toe-nails. He states that they were often markedly transversely ridged, but does not refer to any white lines. He very kindly sent to me the photograph (Fig. 3).

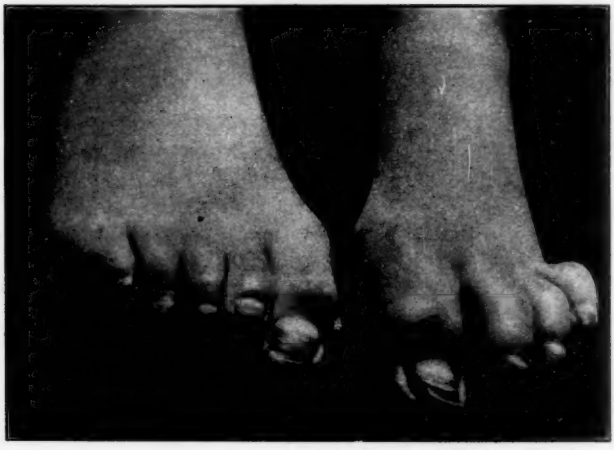
Dr. Leslie Roberts, of Liverpool, writes me that he has not met with such changes herein described, and says, "Temporary arrest of nutrition and formation of air-cavities may produce various markings on the nails."

Dr. Ernest S. Reynolds, of Manchester, who was first to discover and point out the nature of arsenical poisoning due to beer-drinking in England, has very kindly written me under date of May 2, 1903, as follows:

"The white transverse streaks on the nails of cases of arsenical poisoning had already been noted and described by me. (See *Lancet*, January 19, 1901.) Also, you will there find an account of several parallel transverse streaks which I stated would almost suggest a series of drinking debauches.

"I am much obliged for your letter and much interested in it, as it corroborates my own observations. At the time a well-known skin specialist told me he did not think that the transverse streak had anything to do with the arsenical poisoning, but I observed it too frequently for it to have been a mere coincidence."

FIG. 3.



Referring to Dr. Reynolds' article, which appeared in the *Lancet*, January 19, 1901, page 68, in the clinical description, and under the subhead "Nails," I find the following:

"In many cases the nails are affected. After the patients have stopped taking the beer for some weeks the best appearances are seen, for then there is a transverse white ridge across the nails; proximal to this the nail is normal, but distal to it the nail is whiter, cracked, thin, and toward the tip almost papery, and much flattened. In some cases there has been a series of parallel transverse-ridges on the nails almost suggesting a series of week-end 'drinking bouts.' The deformed nails, of course, break easily."

It is to be observed that Dr. Reynolds speaks only of "a transverse white ridge." In my cases and also in Dr. Sabin's there was no well-defined groove or ridge. This difference is possibly due to the fact that his cases were subjected to more prolonged and chronic poisoning by the arsenic. I am nevertheless certain that they are both evidences of arsenical poisoning.

It is possible that careful observation will show that these peculiar markings on the nails quite constantly follow severe acute arsenical poisoning, and I believe they depend upon the serious alteration in the nutrition incident to the profound shock of the poisoning, aided, perhaps, by the specific effect of the arsenic, since I have observed three cases of arsenical neuritis from slow poisoning in which there were no streaks, although the nails were ridged, particularly the toe-nails; nor did I observe in the cases of chronic poisoning that the nails were flecked with little white spots, which are vulgarly called "flowers" or "lies;" they were transversely ridged, pale, brittle, and papery. I do not believe that it is the profound nutritional disturbance alone which produces these transverse lines, since in neither of three cases of severe corrosive poisoning observed after seeing the first case of arsenical poisoning here recounted did white lines develop on the nails; nor has a diligent search through the literature revealed any observations of such changes in the nails following other severe poisoning. It is possible that the arsenic has some specific effect upon a plane of newly developed nail cells within the matrix, and as a result the normal keratinization fails to become physiologically complete.

If my contention is just we have in these nail-markings important corroborative evidence of poisoning by arsenic. The occurrence of these bands following arsenical poisoning is sufficiently established to warrant the use of the term leuconychia striata arsenicalis transversus.

When I began a search of the literature for observations upon the nails it was with some surprise that I found that these transverse white lines had been observed, carefully described, and figured by several authors, but none, excepting Reynolds, ascribed them to arsenic. One recorded case seems to show that they may appear as a congenital anomaly; other observations that they may present, as it were, an unguinal record of a severe illness.

While leuconychia punctata is frequently observed, one may obtain some idea of the rarity of leuconychia striata by the statement of Jules Heller,[1] in his recent work on *Diseases of the Nails*, that it is so rare that but two cases have been thus far reported. In justice to the literature, it is only right to state that Heller is afflicted with the usual literary myopia of German writers, as the following references will evidence:

Reil,[2] in 1792, and Beau,[3] in 1846, published observations upon peculiar changes in the nails due to fevers; also Murchison, in his exhaustive treatise on fevers, alludes to these markings and changes in growths.

Dr. Langdon Down[4] observed two sets of white lines extending transversely over the nails on the fingers and toes of a man who had experienced two attacks of poor health, in each case the lines corresponded with the occurrence of the attack.

Prof. Alfred Vogel,[5] in 1870, and again in 1873, in thorough German fashion, discussed the question of nail changes following fevers, and figured several cases of the white transverse lines in the nails which appeared after typhus fever.

I found a description by Longstreth[6] of transverse white bands extending over the surface of the nails, which appeared after each exacerbation of a case of relapsing fever, recording, as it were, each relapse.

Da Costa[7] also has described such bands appearing after a relapse of typhoid fever, and gives a beautifully colored illustration of a hand the nails of which are traversed with several white bands, each corresponding to a relapse of the typhoid from which the patient had suffered.

Dr. Morrison,[8] of Baltimore, has described a case of transverse white bands on the nails, under the title of "Leucopathia Unguinum," occurring in an otherwise healthy young woman. There appeared a number of these white lines extending from one lateral nail margin to the other, and were about one-sixteenth of an inch apart. No cause for their origin could be ascertained.

Dr. E. J. Stout[9] has reported a case where it appears that a negro had presented such white bands on his nails from birth.

Heidingsfeld,[10] of Cincinnati, has contributed considerable to this subject in a very able article, "Leucopathia Unguinum." He has observed seven well-marked cases of leuconychia striata and nearly double the number of slighter degree. While he does not clearly state that all were due to injudicious use of the cuticle-knife, a "new and somewhat American instrument," I assume, in absence of any mention of other cause operative in his personally observed cases, that each had its origin in tinkering vanity.

He is inclined to disagree with Heller and about all other writers upon the extreme rarity of leuconychia striata. His personal experience hardly warrants his contention, but rather convinces the reader that a very modern use of the cuticle-knife, a comparatively new and certainly vicious instrument, or an unskilful use of it in Cincinnati, is the explanation of his frequent observations. He has made some very interesting and valuable discoveries as to the pathological histology of these striations which seem to overturn the accepted theory of air infiltration. I give his conclusions in his brief recapitulation:

"Leuconychia is the result of some pathological change of structure of a plane of nail-cells, approximating a failure of the affected cells to undergo normal physiological keratinization.

"The cause may be trauma, malnutrition, febrile diseases, neuroses, or any agency which disturbs the growth, development, or keratinization of the matrix cells in their change to nail-structure.

"An infiltration of air is absent, and there is no rational physiological basis for such a theory."

I have given these references to the literature at length for two reasons: First, to show that a thorough search reveals but little upon the subject; a few cases occurring in connection with fevers, some from traumatism; a very few of unexplained origin, and none ascribed to arsenic but by Reynolds. Secondly, as an aid to the diagnosis. Since, if in the presence of such nail changes as here described and illustrated we can exclude congenital anomalies, traumatism, severe illness, especially the acute specific fevers, particularly typhoid, relapsing and typhus, we will be warranted in suspecting arsenical poisoning. And if other corroborating evidences, such as violent unaccountable vomiting, abdominal pain, cramps in the legs and arms, and neuritis can be obtained, I believe we can positively assert that poisoning by arsenic has taken place. And allowing for the rapid growth of the nail following arsenical poisoning, and giving seven months for complete nail-growth, from the position of the white band, we can quite accurately estimate the time of the poisoning.

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A CASE OF PRENATAL APPENDICITIS.

By W. Fred. Jackson, M.D., C.M.,

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This case, being of a very unusual nature, is presented as a contribution to our knowledge of this interesting and prevalent disease.

A female child, fully developed and well nourished, died at 5.30 P.M. from symptoms of metallic poisoning. At the hour of death the child had barely completed forty hours of natal life. At 12.30 P.M. the attending physician saw the infant, and it was perfectly well. Another physician was called hurriedly at 5.15 P.M. the same day, and found the infant collapsed and with a greenish-blue froth issuing from its mouth. This froth and accompanying fluid stained the garments a deep chemical blue. The supposition is that the child died of poisoning by the administration of a blue tablet of bichloride of mercury with citric acid.

A post-mortem examination, which I as Coroner ordered, brought to light the condition of the appendix, as shown in the accompanying illustration, which is taken from a photograph of the specimen.

The appendix is much elongated and congested, lying upon the cæcum, and bound down upon it by numerous and firm adhesions. The surfaces of the appendix, where it is reduplicated upon itself, are firmly bound together. The small intestine and the colon below the ileocæcal opening present no evidence of inflammatory action.

The mother's labor was regular and without incident. The delivery was accomplished with the forceps without injury to the child. The infant was lusty and strong, and apparently perfectly well up to a very short time of its death. How the blue tablet was administered to the child, or by whom, has not been demonstrated.

It seems that the inflammatory condition, as evidenced by the thickened and congested appendix and firm adhesions, must have occurred previous to the child's birth. The more so, as the inflammation was evidently in the stage of resolution.

LUXATIO ERECTA.

By George Tully Vaughan, M.D.,
of Washington, D. C.

Luxatio erecta, a variety of subglenoid dislocation, is so rare that the following case is of interest:

J. M., white, male, aged sixty-six years, barkeeper, was admitted to Georgetown University Hospital October 4, 1903, having just been injured by being struck by a street car. On examination the patient's left elbow was seen pointing upward at an angle of forty-five degrees, the forearm was flexed, with the hand hanging down, dorsal surface toward the patient's face.

The patient could not lower the elbow, even to a horizontal position, although the elbow could be moved inward toward the head to a vertical position without pain. The forearm was placed by me on the top of the patient's head, and the typical attitude of a case of luxation erecta was presented. The head of the humerus was easily felt low down in the axilla. Reduction was effected without trouble after about one minute's extension—seizing the arm with the right hand just above the flexed elbow and making extension upward and slightly outward, while the fingers of the left hand were used to press the head of the bone upward.

No anæsthetic was used and the manipulations were attended with little or no pain.

The patient was last examined November 4, one month after the injury. He could abduct the arm well from the side and carry it across the chest, so as to place the fingers on the opposite shoulder. Flexion of the fingers was possible, but the grasp was quite feeble; extension of the fingers or of the wrist was impossible; there was well-marked "wrist-drop."

He said the fingers felt slightly numb, though rough tests with a pin indicated no difference in the two hands. Flexion and extension of the forearm and abduction and adduction of the arm were well performed.

This variety of subglenoid dislocation of the shoulder was first reported in 1859 by Middeldorpf and Scharm, and up to 1899 Stimson had collected only 9 cases, which, with Middeldorpf's, made 11 cases in all. Of 539 shoulder dislocations observed at St. Thomas' Hospital no case of luxatio erecta was recorded (Makins).

Krönlein reports 3 cases of luxatio erecta in 207 dislocations.

In 400 dislocations Bardenheuer met with no case of luxatio erecta, but saw 2 cases in which the arm was abducted slightly beyond a right angle with the body—luxatio horizontalis—a variety of *subclavicular* dislocation.

REVIEWS.

A Manual of Operative Surgery. By Sir Frederick Treves, Bart., K.C.V.O., C.B., LL.D., F.R.C.S. Second edition. Revised by the Author and Jonathan Hutchinson, Jr., F.R.C.S. 2 vols. Philadelphia and New York: Lea Brothers & Co.

In reviewing a new edition of a work so widely known and so deservedly esteemed as this, it is of chief interest to note the additions and omissions, the changes of opinion, or the confirmation of earlier views wrought by ten years' experience.

In Chapter I. the most noteworthy change is the substitution in place of the remarks on "Cleanliness" of an article on the "Preparation of the Skin." There is perhaps no point in antiseptic technique as to which so much difference of opinion prevails as this, and the method described by the author, who prefers as the chief germicide a 1 : 500 alcoholic solution of mercuric potassium iodide, is not, so far as we know, employed in this country, and is worthy of trial.

In Chapter II. the chief addition is as to matters of *dress*. In this connection the author will probably be regarded by many American surgeons as unduly conservative, and only time and experience will show whether or not he is right. In the mean while his remarks will bring comfort to those operators who doubt the necessity of some of the elaborate precautions now fashionable.

Chapter III., on "The Operating Room," has been expanded and fully illustrated, and now includes a section on "Operations in a Private House," as to which the statement is made that "provided that the greatest care is exercised, there is no reason why as complete asepsis should not be secured in the patient's room as in the most elaborately fitted hospital theatre."

This may be true, but as it is added that "it is in the first place essential that the house be in a perfectly sanitary condition, and as it appears to be an article of the householder's faith that the hygienic state of his or her premises is exceptionally perfect, it is well that the building should be examined by a skilled person without the residential bias;" and that it is desirable that "the room should be quiet, light, and well ventilated," that its windows look toward the south; that it should not be near a water-closet; should have an open fireplace, and should have as little gas burned in it as

possible, it is apparent that the author practically shares the widespread prejudice of surgeons in this country against operations in private houses.

In Chapter IV., the directions for the sterilization of sponges by formaldehyde—misprinted "formal aldehyde"—would seem unnecessary in view of the almost universal preference—which the author shares—for gauze pads.

The omission of the page devoted to an explanation of the abandonment of the steam spray marks one of the milestones in the advance of antiseptic technique. It seems now as if long before 1891—the date of the first edition—the "fort mit dem spray" of the German surgeons had been accepted everywhere.

In Chapter V. a little concession to "blunt dissection" is noticeable, and the teaching seems more in accord with the practice of to-day than the earlier and practically absolute prohibition of such dissection.

On page 71 we note one of the few misprints that we have noticed, viz., "gauge drain" for "gauze drain."

In Chapter VI. the most important addition is found in a paragraph which indicates a change in the methods of wound treatment, and expresses unqualified preference for the practice of keeping the wound absolutely dry from beginning to end. "Micro-organisms cannot grow without moisture, and moist dressings and washing of the wound provide this medium." The details of treatment of an abdominal incision are given, and the author adds: "In my experience no method of dealing with wounds has given such uniformly successful results as this."

In Part II., dealing with the Ligature of Arteries, the previous unqualified opinion that "the best ligature material on the whole is chromicized catgut" has become: "There is considerable choice in the form of ligature used. . . . Kangaroo tendon, catgut, and soft silk of medium thickness may all be recommended."

The author's opinion in favor of the intraperitoneal ligation of the common iliac has been strengthened by further experience. He adds a quotation from Mr. Makins' article on that subject calling attention to the greater anatomical difficulties that surround the ligation of the left common iliac as compared with the operation on the right side.

In Part III., as an addendum to the article on Meckel's ganglion, Mr. Hutchinson—the co-editor of this edition—says: "It is possible that an intracranial resection of the superior maxillary trunk—performed in a similar way to removal of the Gasserian ganglion—may prove to give more lasting results than the operations described."

The article on the Excision of the Gasserian ganglion has been much expanded and the positive statement that "excision of the ganglion by the temporal route is by far the best method, as it

offers a good prospect of permanent cure, and leaves hardly any deformity of the face," is fully justified by the experience of the last few years. The omission of Cushing's method is accounted for (apparently by the co-editor) with the statement that "it is largely a return to the old pterygoid route, involves division of the zygoma, and appears to have nothing to recommend it." Cushing's method is, however, not largely a return to the pterygoid route, and, in the opinion of many surgeons who have employed it, has very much to recommend it. The division of the zygoma is perhaps the least essential part of the method.

In the admirable section on Amputations the only addition to the statistics that we have noticed is a paragraph giving the result of ninety-four major amputations at the London Hospital from 1890 to 1900, with eleven deaths (Mr. Hutchinson). A wider survey of operative results in these cases during this important decade would, we believe, have been of interest and value, although this is not meant in criticism of the mortality (12 per cent.) in this series, which is very creditable.

In the chapter on Interscapulothoracic Amputations no mention is made of the desirability, in some cases of malignant disease, of removing the entire clavicle instead of only the outer two-thirds (Le Conte).

In amputation of the leg the old term as to the "place of election" —a point "about a hand's breadth below the knee-joint"—is employed, although, in this country at least, the point of election has, with the improvement of prosthetic apparatus, descended at least to the junction of the lower and middle thirds of the tibia. No mention is made of an operation now in favor with many American surgeons, in which the tibia is sawn twice, so as to secure a periosteal flap without disturbing the relations of vessels, nerves, and muscles, and so as to prevent the adhesion of the latter to the bone and minimize bone atrophy. It is warmly recommended (Matas, White) and has stood the test of experience.

In the section on Ununited Fracture it is correctly said that "as a practical measure the wire is a delusion and a snare, so far, certainly, as the long bones are concerned;" but when it is added that "the various forms of apparatus in which plates of metal are secured (outside the skin) to the fractured bone by long screws" are "equally fallacious and more dangerous," it would seem impossible to American surgeons that the author—or the co-editor—could be practically familiar with the ingenious Parkhill bone-clamp, here universally regarded as the best of all mechanical devices for securing fixation of the fragments of the long bones after resection of their ends in cases of non-union. The published results obtained in this country amply demonstrate both its safety and its utility.

Volume II. shows fewer alterations or additions. The excellent section on Plastic Surgery remains largely unchanged.

We found no mention of intubation of the larynx in croup or diphtheria. The value of this procedure has been sufficiently demonstrated to justify its inclusion in a work of this comprehensive character, while it can scarcely be dismissed, as might catheterism, as belonging rather to the field of minor surgery.

In describing the operations for hypospadias it would seem as though less space might be given to the elaborate description and illustration of Duplay's and Anger's operations, and more to the very excellent method of Wood, which is criticised, it would seem, on theoretical grounds, and not as a result of practical experience. In the writer's hands the preputial integument has yielded most satisfactory results when used to form the principal flap in this operation, and no trouble has been experienced with "œdema of the lax subcutaneous layer."

A word of caution has been inserted in regard to the term "complete excision" in describing thyroidectomy, attention being called to the absolute necessity of leaving behind some portion of the thyroid gland in all such operations.

In dealing with the surgical accident of the entrance of air into divided veins, the immediate treatment by filling the wound with fluid and expressing air from the chest by direct pressure is described, and the suggestion that air should be sucked out of the right auricle by a catheter passed into the heart is very properly spoken of as "preposterous." When, however, the author adds, "the advice given in nearly every text-book that artificial respiration should be resorted to is almost as silly; there is not too little air in the thorax, but too much," he does not seem to realize that the forcible compression of the thorax to expel the air is only a form of artificial respiration; that the pulmonary circulation must be re-established because otherwise the left heart remains collapsed from want of blood; and that artificial respiration offers the best means of meeting this tremendously urgent indication.

In the chapter on Abdominal Section a useful summary of the arterial supply of the abdominal wall has been added. The statement that the ileocæcal valve corresponds to the spinoumbilical line and that the root of the appendix will be placed more than one inch lower down, and perhaps internally to it, is of interest, but cannot be regarded as demonstrated by the researches of Dr. Keith, to which the writer alludes, and which at present lack confirmation, as does the further statement that the ileocæcal valve in a normal person is usually tender to pressure. The practical importance of the matter is obvious; there are reasons for believing that it is a fact and that it serves to explain some of the too frequent cases in which tenderness elicited by pressure in this region has constituted the chief indication for operation which has revealed a normal appendix.

In addition to the chapter on the Operative Treatment of Enlarged Prostate, the author—or the co-editor—says that castration

and vasectomy in this condition "have been practically abandoned." Mr. Reginald Harrison has reported 100 cases of vasectomy, in every one of which some degree of improvement resulted; and Rovsing, of Copenhagen, has recently (1902) reported 40 cases, of which 27 were cured, 9 relieved, and 4 unimproved. There were no deaths, and he adds, "I should, under no circumstances, feel myself justified in undertaking the total extirpation of the prostate in a patient in whom I had not done a vasectomy, which, in many cases, gives such extraordinary relief." The operations in question have certainly not yet reached their ultimate position in the estimation of the profession. It may be that they will be entirely discarded, but it would seem as though after the expiration of the inevitable period of indiscriminate employment of a novelty (of which Treves has himself complained in relation to the appendix) there would still be a restricted field of usefulness for them remaining; and that the statement that the operations are now practically abandoned is not fully borne out by the facts while men of the professional position of Harrison and Rovsing are still using them.

In the preliminary remarks upon operations on the kidney no mention is made of the two layers of the fat surrounding the kidney (Gerota), recognition of which is of practical value in approaching that organ during an operation.

In describing abnormalities of the kidney, Mr. Morris' more recent figures have not been given; they would, for example, increase the cases of absence or extreme atrophy of one kidney from 1 in 4000 to 1 in 2400 cases. The remaining statistics on this subject are similarly incorrect.

These are all, however, minor matters. The book, as a whole, has not yet been supplanted or replaced by any other single work on the subject in respect to the excellent average judgment that has been displayed in the difficult task of selecting from among thousands of varying procedures those most worthy of description, and in respect also to the simple, clear, straightforward manner in which the information thus gathered has been conveyed to the reader.

J. W. W.

THE PRINCIPLES AND PRACTICE OF SURGERY: DESIGNED FOR STUDENTS AND PRACTITIONERS. Lippincott's New Medical Series. By GEORGE TULLY VAUGHAN, M.D., Assistant Surgeon-General, Public Health and Marine Hospital Service of the United States; Professor of the Principles and Practice of Surgery, Georgetown University. Philadelphia and London: J. B. Lippincott Co., 1903.

THE time has passed when it is possible for an author to present comprehensively in a small single volume the general surgery of

to-day, and yet there is a constant demand for such books on the part of the medical student and the man engaged in the general practice of medicine. It was with the idea of supplying this demand that the present work was prepared. It offers to the reader a condensed, and in most respects a thoroughly satisfactory, presentation of general surgery. The book is quite readable and comprehensive as far as possible in its limited space. It possesses, as such books always do, its points of weakness as well as its points of strength.

In our opinion the chapter on Anæsthetics is distinctly weak, since we feel that this is a subject so little taught in our medical schools that when the student turns to his text-book he should be able to find there all the necessary information regarding anæsthetics, and particularly as regards the method of their administration. The author speaks of bromide of ethyl as a general anæsthetic, although this agent is but little used at present, but he makes no mention whatever of chloride of ethyl, which is being so extensively employed for short operations and as a preliminary anæsthetic to ether. We think also that in the chapter on Fractures too little stress is laid upon the necessity of massage and movement, and particularly is this omission noticeable in the discussion of fractures of the lower end of the radius. We heartily approve of the author's teaching as regards the treatment of strangulated hernia, though we believe that, whenever possible in operating for this condition, a radical cure should be sought rather than the simple reduction of the hernia by the older methods of performing herniotomy. The chapters dealing with Genito-urinary Diseases are more complete than is usually found in single-volume text-books on general surgery.

A general criticism which we feel we must make of this work is the fact that the author has devoted too much space to the older methods of treatment and too little to recent and generally accepted methods, although it is possible that this is wiser in a work intended chiefly for students and general practitioners.

The illustrations are many of them old, although there are also many reproductions of interesting photographs. G.

A PORTFOLIO OF DERMOCHROMES. By PROFESSOR JACOBI, of Freiberg im Breslau. English adaptation of the text by J. J. PRINGLE, M.B., F.R.C.P., Physician to the Department for Diseases of the Skin at the Middlesex Hospital, London. London: Rebman, Limited, 1903.

THE portraits in this atlas, as in a recent French one, have been made entirely after models, the great majority after those in Neisser's collection at Breslau, the remainder after models in the collections

of Lassar and Lesser, of Berlin; Hennig, of Vienna and Baretta, of Paris. A new color-printing process, called *citochromy*, has been employed in their production, for which is claimed absolute accuracy in the reproduction of colors. While the claim of *absolute* accuracy is hardly justified, the appearance of these portraits indicates that the process is much in advance of any of those hitherto employed; we have rarely, if ever, seen more accurately colored pictures of diseases of the skin. The two parts of the atlas thus far published contain 78 portraits on 42 plates, the diseases represented being for the most part selected from among the commoner affections of the skin. The more important and interesting rarer diseases, however, are not omitted, there being excellent portraits of Raynaud's disease, actinomycosis, and anthrax.

Among the plates which especially deserve notice on account of their excellence are those representing various forms of psoriasis, particularly psoriasis gyrata, lupus vulgaris, lupus erythematosus, pityriasis rosea, pityriasis rubra pilaris, and the exanthemata. Two portraits, one representing variola, the other varicella in the adult, are very instructively placed side by side on the same plate. The portrait of scarlatina is most accurate in coloring, but measles is not so successfully represented.

And just here seems the place to say that we have frequently wondered why portraits of the exanthemata do not find a place in *every* atlas of diseases of the skin, since in no class of affections do blunders in diagnosis occur more frequently and result more disastrously.

As the atlas is not designed by its author to take the place of a text-book, the text is considerably condensed. The symptoms of the various diseases portrayed are succinctly and clearly given together with a brief outline of the diagnosis and treatment.

While portraits and models, however well made, can never altogether replace the study of the living subject, portraits as accurate in drawing and coloring as these make very efficient substitutes, and must prove of the greatest service in the recognition of diseases of the skin to those whose clinical opportunities are limited.

M. B. H.

A Text-book of Pathology. By Alfred Stengel, M.D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the Philadelphia Hospital; Physician to the Pennsylvania Hospital. Fourth edition, thoroughly revised. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

That pathology and clinical medicine are intimately related is shown by the fact that one so widely known as a clinician should be so widely read as a pathologist. The usefulness and popularity of this book, especially to the practitioner, is evident when one

considers that four editions have been called for within a period of five years. The book is so well known to pathologists in general that a detailed description is unnecessary. In the present edition numerous revisions and additions have been made, notably in the sections upon typhoid fever, tuberculosis, yellow fever, dysentery, and in the discussions upon diseases of the blood. A short account is given of the latest theories of immunity. In many places the results of the most recent researches in pathology are alluded to, but, as in the earlier editions, references are intentionally omitted. A very wide range of subjects is dealt with and throughout the book special attention has been paid to physiological pathology. In this respect and in many other ways the book is essentially a clinical pathology. An appendix has been added in which one finds a description of the generally accepted methods of pathological and bacteriological technique, and the book justifies in every detail the position which was accorded the former editions. W. T. L.

MANUAL OF THE DISEASES OF THE EYE. FOR STUDENTS AND GENERAL PRACTITIONERS. By CHARLES H. MAY, M.D., Chief of Clinic and Instructor in Ophthalmology, College of Physicians and Surgeons, Medical Department, Columbia University, New York, 1890–1903; Ophthalmic Surgeon to the French Hospital, New York; Consulting Ophthalmologist to the Red Cross Hospital, New York; Adjunct Ophthalmic Surgeon to Mt. Sinai Hospital, New York, etc. Third edition, revised, with 275 original illustrations, including 16 plates, with 36 colored figures. New York: William Wood & Co., 1903.

THIS work contains a clear and terse account of the present state of ophthalmology, so far as this is possible in a book of its size. The reader is never left in doubt as to the writer's meaning. It is easy reading, and we know upon the authority of a famous writer that "easy reading is—hard writing." The author has succeeded in saying enough and not too much, which, as he rightly states in the preface, is the "great difficulty in preparing a book of this sort." Sanity of view characterizes it throughout. One would have to make a somewhat minute search to discover opinions opposed to views now generally held by practical ophthalmologists. We are somewhat surprised at the very little stress laid upon the salts of silver in the treatment of purulent ophthalmia.

This is one of the few books which recognizes that a portion of the accommodation must be kept in reserve during near work, but under the directions for prescribing glasses for presbyopia we do not find that the author is consistent therewith. He subtracts the total accommodation from the amount required for near work and

makes good the deficit by glass, allowing no part of the accommodation to be held in reserve.

A high place (but not too high) is given retinoscopy as an objective test of refraction. In competent hands this is unquestionably the most accurate objective method known, rivalling the best results obtainable by the subjective method under the most favorable conditions. In certain cases it is the only reliable method of determining the refraction. The ophthalmometer is accorded its proper subordinate position in the statement that "it is of service when used in connection with other tests." A mydriatic is recommended in all cases of children and young adults in estimating the refraction. Homatropine is declared to be "*sufficient for all practical purposes*," an opinion with which the reviewer entirely concurs from daily experience.

We note with satisfaction that heterophoria is relegated to a very subordinate place, as in our opinion it deserves. We think that more than enough is granted when neurasthenia, disturbances of digestion and nutrition are set down as possible results of muscular error, even in predisposed individuals; operation is only recommended as a last resort. Disappointment and aggravation of symptoms are truly stated to frequently follow this treatment. The author evidently has little belief in partial tenotomies and advancements. T. B. S.

MANUAL OF MEDICINE. By THOMAS KIRKPATRICK MONRO, M.A., M.D., Fellow of and Examiner to the Faculty of Physicians and Surgeons, Glasgow; Physician to Glasgow Royal Infirmary and Professor of Medicine in St. Mungo's College; formerly Examiner in the University of Glasgow and Pathologist to the Victoria Infirmary. Philadelphia and New York: W. B. Saunders & Co. London: Baillière, Tindall & Cox.

DR. MONRO'S book should serve admirably the purpose for which it is primarily intended: that of a text-book for students. He has accomplished successfully the difficult task of condensing into a volume of moderate size the enormous mass of facts which makes up our present knowledge of internal medicine. The work throughout shows painstaking care in the classification and arrangement of these facts and in their concise and lucid presentation.

In arrangement it does not differ materially from the usual plan of the larger treatises. The space has been judiciously divided, and each section receives its due consideration. This same sense of proportion is seen also in the space allotted to the individual diseases and to their subdivisions of etiology, morbid anatomy, symptomatology, diagnosis, and treatment.

The value of the book to students is considerably increased by the prefacing of most of the sections with introductory chapters upon the topographical anatomy, general symptomatology, and methods of examination of the subject in hand.

The section on Diseases of the Nervous System merits especial commendation for its completeness and for the clearness with which the subject is treated.

Somewhat less full and satisfactory are the chapters upon Diseases of the Stomach. For some reason the subject of Hemorrhage from the Stomach is not considered, although a corresponding chapter appears under Diseases of the Intestines. The somewhat surprising statement is met that epithelioma is one of the four anatomical types of cancer of the stomach!

In addition to the sections usually found in text-books on medicine there is a short but adequate one on Diseases of the Skin.

L. A. C.

A Surgical Hand-book for the Use of Students, Practitioners, House Surgeons, and Dressers. By Francis A. Caird, M.B., F.R.C.S. Ed.; Assistant Surgeon, Royal Infirmary, Edinburgh; and Charles W. Cathcart, M.B., F.R.C.S. Eng. and Ed., Surgeon Royal Infirmary, Edinburgh. With very numerous illustrations. Twelfth edition. London: Charles Griffin & Co., Limited. Chicago: W. T. Keener & Co., 1903.

As the authors say in their preface, they have endeavored to make this little work of some three hundred pages as practical as possible and as thoroughly in keeping with modern surgical methods as the size of the volume will permit. The mere fact that it is in its twelfth edition is a warrant as to its popularity, at least on the other side of the water. In this edition a number of methods of treatment which are now seldom used have been dropped, and instead have been inserted accounts of the latest technique. It is really worthy of note the amount of useful information the authors have been able to put in such a small book, preserving at the same time the necessary clearness of description.

All minor surgical operations are fully covered and many major ones, while the chapters on dressings afterward and emergency work are most admirable. The illustrations are mostly woodcuts and are diagrammatic, but are clear and show well what is intended. They are very numerous. Special chapters on Surgical Electricity, Massage, Urine Examination, and Post-mortems seem a little out of place in a work of this character, but are well written and of interest. Written, as it is, as an aid to hospital internes and students, it is excellent and to be highly commended. G. M. C.

THE MEDICAL EPITOME SERIES. ANATOMY: A MANUAL FOR STUDENTS AND PRACTITIONERS. By HENRY E. HALE, A.M., M.D., Assistant Demonstrator of Anatomy, College of Physicians and Surgeons, Columbia University, in the city of New York. Series edited by V. C. PEDERSEN, A.M., M.D. Illustrated with 71 engravings. Philadelphia and New York: Lea Brothers & Co., 1903.

THE books of this series are designed by the editor to represent more than the mere quiz compends—to be, in fact, brief manuals of condensed useful information on their respective subjects.

They have, however, for quiz purposes, a list of questions at the end of each general division which serves rather as a guide to the quiz-master than to furnish him actual questions and answers, as is often done, and in which case the continuity of the text is interrupted. This work on Anatomy is clear, concise, and presents more than the mere essentials of human anatomy. It is well written and well printed, while the illustrations are most excellent—far better than those usually seen in short works of this character—and the explanatory notes are clear and well adapted to show the desired point. It is a very good and useful little book. G. M. C.

A TEXT-BOOK UPON THE PATHOGENIC BACTERIA. FOR STUDENTS OF MEDICINE AND PHYSICIANS. By JOSEPH MCFARLAND, M.D., Fourth edition, rewritten and enlarged. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

DURING the five years which have passed since the last revision of Dr. McFarland's book much new material has been collected, and the present edition shows the care with which this material has been added and welded into the text. The many references to literature give the book a certain value. The subjects of infection and immunity have been expanded at some length and in places detailed descriptions are given of recent work along these lines of investigation. The chapters upon the pathogenic bacteria are arranged under four main heads: (*a*) "Phlogistic Diseases," including "Acute Infective Inflammations" and "Chronic Inflammatory Diseases;" (*b*) "Toxæmias;" (*c*) "Bacteremias" and "Miscellaneous Diseases." Each chapter represents a consideration of the disease or pathological processes caused by that organism, as well as a description of the organism itself. When necessary, closely allied bacteria are also discussed. Since the book deals simply with bacteria, the parasites and protozoa are necessarily omitted. Revisions and additions have been made in various portions of the text, and the present edition will perhaps attract even more attention than the previous ones. W. T. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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Ochronosis: The Pigmentation of Cartilages, Sclerotics, and Skin in Alkaptonuria.—OSLER (*Lancet*, January 2, 1904, p. 10) reports two cases of ochronosis in patients also suffering from alkaptonuria. This rare condition was first described and named by Virchow in 1866. A man, aged sixty-seven years, died of aneurysm, and at autopsy it was found that there was a remarkable blackening of the cartilages of the whole body. The color was coal black, not ochre-colored or yellow. It was more than an ordinary melanosis. Previous to Osler's two cases there have been only seven instances reported in the literature. Two of these cases had melanuria, and in one of them it was definitely stated that the patient did not have alkaptonuria. The seventh case was reported by H. Albrecht in 1902, and to him is due the credit of first suggesting the association of the condition with alkaptonuria. The urine of his case was dark-colored and reduced copper-sulphate solution, but no homogentisic acid was definitely demonstrated in it. The necropsy in this case showed a general ochronosis. A point of special interest was the gray-blue color of the inner part of the ears, as if due to dilated veins.

Osler's two cases of ochronosis are of especial interest in that the condition was recognized clinically, owing to the pigmentation of the sclerotics and cartilages of the ears, and in one by a remarkable ebony-black discoloration of the skin of the nose and cheeks. Both of these cases had previously been reported as instances of alkaptonuria, the urine of both showing all the features characteristic of this anomaly. The two patients were brothers. The first is a man, aged fifty-seven years, and the pigmentation now presents the following distribution: The exposed portion of the sclerotics of both eyes show areas of deep-

black pigmentation. The cartilages of both ears, particularly the concha and antihelix, exhibit a remarkable blue-black discoloration. Of particular interest in this case is the fact that over the nose and cheeks there is a butterfly-shaped area of black pigmentation of the skin. The pigmentation closely simulates the appearance of powder marks. The involvement of the skin has not been previously recorded. The pigmentation had been observed for eight years and it had gradually deepened. The other brother, aged forty-nine years, presented similar pigmentation of the sclerotics and ears, although in a less marked degree. He recently died of some cardiac affection, but no autopsy was obtained. Both patients had had alkaptonuria for many years, and there was no question but that the pigmentation was that of ochronosis. Alkaptonuria heretofore had been recognized clinically only by the urinary changes. These observations leave little doubt that ochronosis is a part of the malady. At least one of the previously reported cases of ochronosis was proven not to be an alkaptonuric, and A. E. Garrod suggests that there may be two distinct classes of the condition.

Multiple Myeloma (Myelomatosis) with Bence-Jones Proteid in the Urine (Myelopathic Albumosuria of Bradshaw, Kahler's Disease).—F. PARKES WEBER (*Journal of Pathology and Bacteriology*, December, 1903, p. 173) reports a case of albumosuria in association with multiple myelomata. The patient was a man, aged fifty years, with a definite luetic history. He complained of pain in his loins and of stiffness in the small joints of his hands. Later the upper part of his back began to bend, so that he always stooped. There were no localized outgrowths projecting from the bones, as has been observed in many of the cases reported. The urine contained the so-called Bence-Jones bodies. It coagulated at about 58° C., at a temperature much lower than ordinary albumin does; the precipitate almost completely dissolved on raising the urine to the boiling-point, and completely on adding acetic acid, and reappeared on cooling. An interesting feature was the fact that the proteid was occasionally precipitated spontaneously and caused the urine to be turbid when freshly voided. The autopsy showed that there were no localized bone tumors, but that there was a diffuse myelomatous involvement of the marrow of all the bones examined. There was a chronic ulcer of the duodenum, which has led to a severe hemorrhage, causing death.

The presence in the tumor cells of certain granules and globules of various sizes constituted a striking histological feature in the case. Prof. R. Muir, of Glasgow, who examined the growth, expressed his opinion as follows: "That the tumor is formed by a special and characteristic type of cell, which is probably derived either from the neutrophilic myelocyte or its predecessor; that the cell produces in its protoplasm, in a granular form, a substance which is closely allied to, though not quite identical with, the substance of the neutrophile granules; and that this substance is formed in excess and may form larger granules by confluence of the smaller, the larger globules sometimes becoming free."

The nature of the Bence-Jones bodies is considered at some length. The view advanced by Magnus-Levy, that it is a non-assimilated digestive proteid, is opposed, because in this case alteration of the diet had no effect on the excretion of the albumose, and as much was eliminated during the night as during the day. The view that this proteid is pro-

duced in the bone-marrow is supported, and the suggestion is thrown out that the curious granules found in the specific cells of the tumor may possibly be its source.

Weber has collected the cases of Bence-Jones' albumosuria from the literature, and finds that, including his own, there have been thirty-five undoubted instances recorded. In addition to these there were four doubtful cases.

Family Diabetes.—MARTINET (*La presse médicale*, February 10, 1904, p. 94) reports that in June, 1900, a man, aged forty-eight years, consulted him for symptoms which proved to be those of diabetes mellitus. The disease had followed an attack of influenza contracted in the previous February. The patient's father had died of diabetes also.

Several months later the writer was consulted by the patient's wife, a woman aged forty years. She was found to have exophthalmic goitre. The examination of the urine showed a large amount of sugar present. Martinet considers this a typical case of *conjugal diabetes*, although some objection might be taken to this opinion, owing to the not infrequent occurrence of glycosuria in exophthalmic goitre. He states that he observed four cases of conjugal diabetes in his practice during the year 1903, and does not believe that the condition is extremely rare.

At the beginning of this year the mother of the first patient, aged sixty-six years, came under treatment for a phlegmon on the right hand, which developed very rapidly after being pricked with a needle. The examination of this patient's urine also showed abundance of sugar. She lived with her son.

In this family the patient, his mother, and his wife had diabetes and his father died of the disease. The writer lays down the following axiom: If one discovers diabetes in one or several members of a family, the urine of all the other members should be examined for sugar, especially if the various members live together.

The Reactions of the Blood in Diabetes Mellitus: A Contribution to Our Knowledge of the Thermolabile Complements.—SWEET (*Journal of Medical Research*, October, 1903, p. 255) carried out a series of experiments with the view of ascertaining, if possible, the cause of the abnormal susceptibility of diabetes to infectious processes. The experiments were made on the blood of dogs rendered diabetic by the extirpation of the pancreas. The washed red cells of guinea-pigs and rabbits were used for testing the hæmolytic activity of diabetic dogs' serum. His experiments seem to afford the first adequate explanation for the frequency of infections in diabetes mellitus.

The writer's more important results may be summarized as follows: The complete removal of the pancreas from dogs, which causes a true diabetes mellitus of a severe type, is followed by a marked decrease of the hæmolytic activity of the diabetic dog's serum for both rabbit's and guinea-pig's erythrocytes. The diabetes caused by the complete extirpation of the pancreas is further characterized by what is to be interpreted as a complete loss of the normal bactericidal property of the serum of the dog. This he demonstrated conclusively for *B. coli communis*, *B. typhi abdominalis*, and for *B. dysenteriæ*. The demonstration of the decrease of bactericidal power of the diabetic serum for *staphylococcus pyogenes aureus* was not so conclusive, for the reason that the normal

serum of the dog has very little if any bactericidal effect upon this organism. The decrease of the hæmolytic activity of the serum of the diabetic dog is due to loss of hæmolytic complements. The loss of bactericidal power is, from analogy with the hæmolytic phenomenon, doubtless to be interpreted as due to a loss of bacteriolytic complements. The complete removal of the pancreas is as necessary to this loss of complements as it is to the production of a diabetes. The complete removal of the pancreas does not deprive the organism of its power to react to the inflammatory process by an increase of the complementary substances. The loss of the complementary substances in diabetes mellitus points conclusively to the fact that no relation exists between the leukocytes of any type and the production of the complements.

SURGERY.

UNDER THE CHARGE OF

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On the Use of Rubber and Thread Gloves.—GOEPEL (*Centralblatt für Chirurgie*, 1903, No. 42) states that in view of the fact that rubber gloves tear very easily and that thread gloves are very permeable, it is a good procedure to wear the latter over the former, which not only prevents the slipping of instruments, etc., but also has the following advantages: 1. It is a greater safeguard against infection, either of the patient by the operator or *vice versa*. 2. The hands can be used more freely and easily. 3. The gloves can be rapidly changed should necessity require. 4. The use of the thread glove does quite away with the slipperyness of the rubber, and so ligatures may be tied more easily and securely. 5. The thread gloves can be easily removed in any case where their roughness might injure the tissue and then be replaced when the danger is passed. 6. The time of the operation is shortened. 7. By their use repeated washing of the hands becomes unnecessary, as the gloves can be scrubbed while on the operator's hand, and this prevents chapping or eczema in those cases where the hands are very sensitive.

Three Cases of Rupture of the Intestines without External Lesion.—SENEREANO (*Bull. et mém. de la Soc. de chir. de Bucharest*, 1903, Nos. 3 and 4) states that during the past year he has had three such cases present themselves for treatment, respectively, twelve hours, twenty-four hours, and thirty-eight hours after the receipt of the injury. The first patient had an old and reducible right-sided hernia, and gave a history of having received a sharp blow in the right iliac fossa. He

entered the hospital on the next day, and in the afternoon was given a purgative. The next day he was in a very grave condition, presenting the symptoms of an intestinal lesion, but nothing characteristic. An exploratory incision was made as for hernia or appendicitis; the hernial sac was found empty and there was no strangulated intestine. The incision was then enlarged, the cæcum and appendix were found to be normal, but the entire abdominal cavity was filled with intestinal contents, and 25 cm. from the cæcum was a perforation which admitted the little finger. This was closed, thorough lavage of the abdominal cavity was then performed and the wound closed; the patient made a good recovery. The second case had an old and reducible hernia upon the left side. He was kicked in the abdomen by a horse and twenty-four hours later was admitted to the hospital. Upon operation on the third day, it was found that there was a perforation of the small intestine, and that the abdominal cavity was filled with intestinal contents. The perforation was closed, the abdominal cavity irrigated, and then the wound closed. The patient recovered. The third patient had no hernia, but had received a blow upon the abdomen, which was opened in the median line. Two perforations were found near the cæcum about 8 cm. apart. They were closed and the abdomen washed out. This patient also made a good recovery.

Actinomycosis of the Liver.—AUVRAY (*Revue de chir.*, 1903, No. 7), after an admirable and exhaustive review of the subject, states that medical treatment by the iodide of potassium has proven to be of no value in these cases. Although the number of cases is small, still, it may be well said that this treatment has been followed by good results when the disease is localized elsewhere, and in every case it would seem to be a valuable adjunct of the surgical treatment. The author reports the surgical treatment of six cases in which the liver was involved, but it is to be regretted that some of these reports are quite incomplete as regards the exact operative procedure in the individual case. These cases all presented some form of abscess, and there are three ways of reaching and evacuating such a purulent collection: 1. By way of the abdomen, the usual method. 2. The thoracic route. 3. The lumbar route. In four of the cases the abscess was opened through the abdomen, in some the operation merely consisted in a simple incision of the abdominal wall, while in others a formal laparotomy was necessary, with a resection of the ribs in an effort to discover the exact point of the infection. The only complication during these operations was in one case in which there was an abundant hemorrhage. The lumbar route was used in only one case; the incision was made parallel to the last rib, and then the abscess was punctured with a trocar and evacuated. The thoracic route was followed in one case without a previous resection of the ribs. These six cases were all eventually fatal, but not as the result of the operative interference; the results might have been better had the operations been performed earlier—in other words, before the formation of an abscess.

Suture of the Patella: A Practical Study Based upon Seventy Operations.—LUCAS-CHAMPIONNIERE (*Archives internationales de chirurgie*, 1903, No. 1) states that the first antiseptic operation of suturing of the patella was performed by Cameron, of Glasgow, in

1877. At this time Lister also reported his first case, and in 1883 he was able to note six more, and clearly showed that this new method of treatment was followed by a perfect recovery, whereas in the past the condition had been looked upon as being of necessity followed by lameness. In view of the fact that fracture of the patella is comparatively rare, the author's experience of seventy cases is quite remarkable. A study of these cases shows that the only rational method of treatment is a free incision of the joint; the evacuation of its morbid contents, such as blood; the accurate apposition of the fragments by suture, and then the repair of the torn synovial membrane, and this is the only way in which good union can be secured. The best suture material is silver wire, which is in itself antiseptic. Care should be taken to have absolute asepsis, and the joint should be thoroughly flushed out with a 5 per cent. solution of carbolic acid. The best time to operate is either two, three, or four days after the accident, and not within the first twenty-four hours. The wound should be drained for four days, and there should be passive motion at each dressing. The patient should be allowed to walk in from ten to fifteen days. In conclusion, the author reports in detail many of the more interesting and complicated cases of the series.

THERAPEUTICS.

UNDER THE CHARGE OF

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Light Therapy.—Dr. Kellermann considers that the use of dark-blue incandescent light produces excellent results when locally applied in neuralgia and eczema, and his statistics seem to prove his assertion. He also states that the treatment may be applied in leg ulcers. The duration of each treatment is not more than fifteen minutes and the number of sittings should not be more than four per week. He believes that the beneficent effect is due chiefly to the action of dry heat, and that the chemical or specific action of the light rays plays a very subordinate part in producing the result. His article contains a report of numerous cases which have undergone the treatment.—*Zentralblatt für die gesamte Thérapie*, 1904, No. 1. p. 16.

Serum Therapy in Plague.—Dr. Victor Godinho, in his plague service at the hospital in San Paulo, Brazil, has employed a serum made after the manner of the plague serum prepared at the Pasteur Institute, and reports upon its use as follows: The minimum dose injected was 150 c.c. to 200 c.c. When injected during the evolution of the disease no abortion of the malady took place and the buboes appeared as usual, but their pain was lessened and sudorific crises and defervescence by lysis were produced. Intravenous injections of 20 c.c. to 40 c.c. of the

serum would cause a rise in temperature of a degree, followed by abundant perspiration and a fall of two or three degrees. In some patients it seemed as if the crisis of the disease was brought about by the serum, since the temperature fell and did not rise again after its use. Certain transitory symptoms, such as chill, agitation, dyspnœa, cyanosis, vomiting, etc., were caused by the injections. When administered before the third day of the disease the serum almost always brought about a cure in adults, but did not influence the development or the suppuration of the buboes. The course of the disease being much more violent in children makes it imperative that the serum should be used as early as possible. The occurrence and course of pneumonia as a complication did not seem to be influenced by the serum. Those suffering from the septicæmic form of the disease bore the serum well, but its good effects were less marked than in those affected with the bubonic type. Lastly, the serum did not prevent the termination of the disease by cachexia. In conclusion, the author states that the use of the serum, like that of diphtheria antitoxin, results favorably in certain cases, but not in all.—*La presse médicale*, 1904, No. 8, p. 60.

Suprarenal Opotherapy.—Dr. A. Goy states that in connection with this subject the following conclusions have been reached: 1. That the administration of the suprarenal extract slows the pulse by stimulating the pneumogastric. 2. That it strengthens the cardiac systole by direct stimulation of the heart muscle and by stimulation of the cardiac ganglia. 3. That it causes an increase in blood pressure due to contraction of the capillaries through stimulation of their vasomotor nerves and muscle fibres and by action upon the vasomotor centr . 4. That it blanches and causes an anæmia of the tissues. The primary therapeutic application of the extract is in Addison's disease and in the treatment of certain symptoms of suprarenal insufficiency. In Addison's disease in a short time the extract causes a diminution in the pigmentation and a rapid increase in body weight. In experimental physiology the extract has been employed as an intravenous injection as an heroic remedy in animals in chloroform syncope. An important consideration is that the preparation used should be of definite strength. —*Revue francaise de médecine et de chirurgie*, 1904, No. 3, p. 64.

The Treatment of Hepatic Colic.—The indications to be met in this condition are these: to relieve the pain; to bring about a favorable issue of the crisis by facilitating the passage of the calculus; to prevent complications. The pain may be relieved by the hypodermic use of morphine in connection with atropine. This latter should be most carefully given when there is tendency to collapse. To patients who bear morphine badly chloroform to the obstetrical degree may be given, or if there is no vomiting the following formula: Chloral hydrate, 2; syrup of peppermint, 30; chloroform-water, 100. Dose, two dessertspoonfuls every quarter-hour until relieved. When the stomach is intolerant the chloral may be given per rectum, thus: Chloral hydrate, 2 to 3 parts dissolved in 10 parts boiling water mixed with the yolk of an egg, to which mixture 1 part of wine of opium and 200 parts of milk are added. Ether and turpentine, on the one hand, and olive oil and glycerin, on the other, are the remedies most usually employed to facil-

itate the passage of the stone. The latter agents are preferable. The great difficulty is to overcome the repugnance of the patient to the olive oil. Toward this end the oil may be stirred up with a little beer, or to it may be added a little menthol or a few drops of essence of bitter almonds or anise. The quantity of the oil should be from four to eight ounces. Glycerin is more acceptable to the patient, but less effective. Finally, the spasm of the bile-ducts may be relieved by the application of hot-water bags to the abdomen. Of the complications of hepatic colic, the most formidable is heart-failure. To combat this it is wise to substitute for the atropine, so frequently given with the morphine, a heart stimulant, such as sparteine. Chloral should not be given where collapse is threatened, and in this juncture hypodermic injections of camphor in olive oil are useful. To prevent accidents to the biliary passages, we should avoid the use of purgatives and suspend food until the pain has ceased for several hours. Rupture of the bile-passages necessitates immediate surgical interference.—*Revue francaise de médecine et de chirurgie*, 1904, No. 5, p. 115.

Iodized Oil in Simple Goitre.—Dr. Dubar reports two cases of simple goitre in young girls which he has treated by injections of oil containing 40 per cent. of iodine. He injected very slowly at intervals of about one week fifteen drops of the oil into the substance of the gland. Each injection was made into a different part of the gland, and while in no case was there any unpleasant reaction, two or three of the injections were followed by the appearance of a small, firm node showing no signs of inflammation. These eventually disappeared. In one patient, after a series of nine injections, the size of the goitre was diminished by three-fourths of an inch. In the other six injections resulted in a diminution of nearly one inch, and a series of four more injections caused a total shrinkage of nearly an inch and one-half.—*Le progrès médicale*, 1904, No. 4, p. 50.

Sodium Bicarbonate in Gastropathies and Other Diseases.—M. Henri Huchard, in a paper upon dyspepsia, deals at length with this therapeutic agent. In anorexia he believes it to be indicated in small doses (3 to 5 grains), since, taken a half-hour before eating, it increases gastric secretion and excites the contractility of the stomach. In this connection he considers it far preferable to the bitters. In hyperchlorhydria, since here we have an excess of gastric secretion, the drug should be prescribed in large dosage at the end of the period of digestion, at about the time when the gastralgia is likely to appear—that is to say, about two or three hours after the meal. In this condition the author gives 4 or 5 drachms daily of the salt for several weeks at a time, and finds no resulting evil effects; on the contrary, oxidation and metabolism are favored, and an increase in body weight often takes place. The gastric crises of tabes, when these are accompanied by hypochlorhydria, respond well to sodium bicarbonate given in doses of 5 drachms per day. Also the drug produces excellent results in the migrainiform affection termed nervous gastrotoxia. Undoubtedly, when the drug is given improperly, various bad effects may follow; even anæmia may be produced, but these results are not to be considered the fault of the alkali, but of the prescriber. Sodium bicarbonate is the remedy *par excellence* in diabetes, in the prevention of coma, which condition is

characterized by a true acidæmia. The dosage in this disease should be at least 2.5 drachms daily, and where coma actually exists as large a quantity as 3 ounces may be given. In dermatoses, especially those of arthritic origin, alkaline medication has a distinct sphere, and in such conditions the bicarbonate is indicated in doses of 3 or 4 drachms per day. In biliary lithiasis and hepatic colic there is, in the author's experience, no surer method of cure than regular alkaline medication employed in massive doses.—*Revue de thérapeutique*, 1903, No. 2, p. 37.

The Treatment of Thrush.—Dr. Merletti has found that the treatment of this affection by successive applications of hydrogen dioxide and sodium borate solutions is to be recommended. These two agents produce an abundant froth, which acts rapidly upon the *oïdium albicans*. The author has employed this procedure in a great number of cases, and is convinced that, when repeated three times every twenty-four hours, it will bring about a cure even in marked cases of the confluent type of the disease. If the treatment is instituted at the beginning of the affection two or three applications are sufficient to stop the growth of the fungus.—*Journal de médecine de Paris*, 1904, No. 4, p. 31.

OBSTETRICS.

UNDER THE CHARGE OF

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The Induction of Labor for Contracted Pelves.—In the *Archiv für Gynäkologie*, Band lxx., Heft 3, 1903, Hahl gives the result of 84 cases in the Obstetric clinic of Helsingfors in which labor was induced for contracted pelvis. His statistics cover the practice of the Clinic for thirty-two years and the cases occurred among 23,000 patients. The relative frequency of the operation was one in 274 confinements, or 0.365 per cent. In Leopold's clinic the operation was done once in 131 patients, and in a subsequent series of cases once in 151 patients. Braun's statistics give one in 441 patients; Chrobak one in 627; Pinard one in 150, and Walter one in 165.

The smallest true conjugate in these cases were 7 cm. in three and 7.5 cm. in one case, a flattened and symmetrically contracted pelvis. The earliest period of gestation at which pregnancy was interrupted was thirty weeks in one case, and the latest thirty-eight weeks in seven cases. The average was from the thirty-fifth to the thirty-sixth week.

In seven cases the fœtus was in a transverse position. This was corrected by version or spontaneous evolution. The complications which occurred during the labors were transverse presentation in 5 cases, breech presentation in 2, prolapse of the cord in 3, lateral placenta

prævia in 1, and threatened rupture of the uterus in 1; 29.76 per cent. of the cases terminated in spontaneous birth; 70.24 per cent. required operation. Version was done most frequently and then forceps. Craniotomy was performed but twice, or 3.38 per cent.

The results of this series of cases were as follows: The maternal mortality was 2.38 per cent. from all causes. From septic infection alone the mortality was 1.19 per cent. The maternal morbidity was 7.23 per cent. Of the 84 children, 75 per cent. were born living and 25 per cent. were stillborn; 59.52 per cent. were discharged living from the hospital, while 13 of the 63 children born living died in the hospital during the first two weeks. Of the children who left the hospital living, 84 per cent. survived for a year, which was one-half the entire number of children born alive.

Mechanical Dilatation of the Cervix during Pregnancy and Labor.—De Seigneux (*Archiv für Gynäkologie*, 1903, Band lxx., Heft 3) criticizes Bossi's dilator because it has no pelvic curve, cannot be taken apart for cleansing, and cannot readily be shifted to vary the line of application of its force during its use. To correct these faults, he has invented an instrument resembling Bossi's in its general principles, having a pelvic curve and which can be taken apart for cleansing and whose branches are so placed upon the joints that they exercise force in various directions. He reports seven cases in which his instrument was used by himself and others with satisfaction.

Prolapse of the Placenta from its Normal Situation.—In the *Archiv für Gynäkologie*, 1903, Band lxx., Heft 3, Kayser reviews extensively the literature of this subject. He finds in the records of the Clinic at Dresden no case of prolapse of the placenta recorded in 22,000 births. In the Clinic at the Charité there was recorded no case in 42,800 births. On examining the records, a case of version with bleeding is described which must have been a prolapse of the placenta. A few cases collected from the literature are quoted in which this accident happened.

His own case was that of a multipara, aged thirty-three years, who had a considerably contracted flattened pelvis. Eight hours after the rupture of the membranes, the head presenting, fetal heart sounds became much less frequent. On examination, the placenta was found presenting at the internal os, although formerly it could not be discovered. There was slight hemorrhage. Prolapse of the placenta was diagnosticated and version was performed, which was accompanied by a slight discharge of blood. The fœtus was not extracted, but was allowed to remain in the uterus in the hope that labor pains would come on. Fifteen hours after the performance of version the patient was found in collapse and shock. The cervix was incised. The body of the child was delivered with difficulty and the head was delivered by craniotomy. The patient died during the operation. Upon autopsy the attachment of the placenta had been at the fundus of the uterus. A transverse rupture of the uterus was found on the anterior wall of the cervix, while upon the right side was discovered a dermoid cyst. It was Kayser's belief that the rupture of the uterus occurred while an assistant made strong pressure upon the after-coming head in an effort to press it downward into the pelvis.

From the cases reported and from his own, Kayser deduces the

following conclusions: In the presence of prolapse of the placenta with hemorrhage, delivery is imperative. A high degree of pelvic contraction forbids the performance of version. Embryotomy is usually indicated.

If hemorrhage be absent and the child be living, an effort should be made to save its life. Delivery should then be conducted in the manner least dangerous for mother and child. If the child is dead and the pelvic measurements are normal, immediate interference is unnecessary.

A Contribution to the Etiology, Symptomatology, and Treatment of Ectopic Gestation.—RUNGE (*Archiv für Gynäkologie*, 1903, Band lxx., Heft 3) reports 233 cases of ectopic gestation from the Charité and Polyclinic in Berlin. There were 125 cases of recognized pregnancy and 108 cases of hæmatocele. Among the cases of pregnancy, 73 were tubal abortions, 47 ruptures of the tube, and 5 intact tubal pregnancy. Among the unusual cases were one treated by posterior colpotomy in which the tube was removed with the ovary; one case of interstitial pregnancy; one case of ectopic gestation in which a living child was delivered by abdominal section, the child surviving and the mother afterward dying from purulent peritonitis, and one case of tubal abortion with suppuration.

So far as the results were concerned, from the 73 cases of abortion, 36 recovered without operation and 36 recovered after operation. One case died after operation. In 47 cases of rupture of the tube, five were treated without operation and recovered. Forty-two were operated upon, of whom 31 recovered and 11 died. This gives a mortality of 1.4 per cent. in tubal abortion, and 23.4 per cent. in ruptures of the tube. Eight of the deaths resulted through anæmia from hemorrhage and 3 from septic infection. In one case the cause of death could not be distinctly made out. The entire mortality for cases of rupture, excluding those dying upon the operating table, was 6.4 per cent.

In 108 cases of hæmatocele, 37 were treated by operation; 25 of these were done by incision through the posterior wall of the vagina. Seventy-one cases were treated without operation, and of these one died. This patient perished from purulent septic peritonitis. One patient died after operation from infection of the hæmatocele.

Runge's conclusions in the study of his cases are as follows: He believes that the principal causes for tubal gestation are infection during the puerperal period and gonorrhœa. It is, however, true that women who have not been previously pregnant are not exempt from ectopic gestation. A period of sterility in most cases precedes the period of ectopic gestation. Tubal abortion and rupture occur most frequently from the first to the third month of pregnancy. In these cases operation is to be undertaken when conditions threatening life arise, when the tumor increases rapidly in size, when the general condition of the patient grows worse and resorption of the tumor does not occur, and when the patient has long-continued fever. Abdominal section without drainage is best for these cases and the placenta and fetal sac should be removed entire if possible. Only those blood clots which can be readily reached should be removed unless the blood is decomposed and infected. In view of the risks of abdominal pregnancy, it is not well to wait until the child is viable.

Hæmatocele should, if possible, be treated without operation. The

method of election is by incision of the posterior vaginal wall, abdominal section being reserved for those cases in which the tumor is large and in which it cannot safely be reached through the vagina.

The Morbidity of the Puerperal State in Cases Complicated by the Birth of a Macerated Fœtus.—KOTHEN (*Archiv für Gynäkologie*, 1903, Band lxx., Heft 3) reviews the literature of the subject, in which he has collected 358 cases of labor complicated by death and maceration of the fœtus. In 34 of these cases some complication arose during the puerperal period. A morbidity of about 10 per cent. was observed. The second series of 274 cases was observed, 157 of which made normal recoveries, although the fœtus had been considerably decomposed. Spiegelberg ascribed morbidity in these cases not to the death of the fœtus, but to outside contamination in the conduct of labor. Klein injected into animals an extract of the tissues and organs of a fœtus which perished about fourteen days before its birth. Two animals died after such injection. The symptoms of death were those of toxæmia, as the injected material was proved by culture to be sterile of bacteria.

Kothen's cases were 70 in the Clinic at Giessen. Fever was considered present when the patient's temperature rose above 99.5° F. at any time. In 14 of these cases, or 20 per cent., the temperature rose. In 27.1 per cent. some abnormality followed the birth of a macerated fœtus. In comparison with the general morbidity of other puerperal patients, the death and maceration of the fœtus increases the complications of the puerperal period by 10 or 11 per cent. In none of these cases was the death of the mother traceable to a macerated and dead condition of the fœtus.

Kothen concludes from a study of this subject that an increased morbidity of from 10 to 11 per cent. over the ordinary morbidity of labor and the puerperal state is observed in cases where the fœtus is macerated. A foul condition of the lochia is apt to be present in these cases.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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New Method of Ventrosuspension.—BARDESCU (*Zentralblatt für Gynäkologie*, 1904, No. 3) describes the following method of suspension of the uterus: The uterus is drawn upward with a volsellum after the separation of adhesions. An incision is made through the fascia and rectus muscle on either side of the wound, and each round ligament is seized in turn with a bullet-forceps and the loop is drawn through

the opening and secured with four catgut sutures. The fascial edges are then united, after which the loops are sutured together in the median line. The patient is kept on her back for ten or twelve days, the urine being drawn by catheter until the third day.

Care should be taken not to elevate the fundus uteri above the symphysis, or to approximate it too closely to the abdominal wall, in order to preserve the normal relations and mobility of the organ.

Causes of Sterility.—In a discussion of this subject before the Dutch Gynecological Society (*Zentralblatt für Gynäkologie*, 1904, No. 3) KOUWER stated that in 700 private cases sterility was noted in 101, 11 being due to impotence in the husband. The speaker had been successful in treating less than one-half of the cases in which this was the main symptom for which relief was sought (24).

Treub had noted 39 cases out of 188 in which the husband was at fault. In 80 cases occurring in married women where the semen was examined, he found azoöspermia in 25 and oligozoöspermia in 12. The speaker said that he always examined the husband's semen if possible.

Lysol Poisoning.—HAMMER (*Münchener med. Wochenschrift*, 1903, No. 21) reports several cases in which intrauterine injections of lysol solution were followed by unpleasant results. From experiments on animals, he concluded that the use of strong solutions was not advisable. In a puerperal case fatal thrombosis occurred from the entrance of lysol into a vein (the strength of the solution was not stated).

Torsion of the Uterus.—PETIT (*Semaine gynécol.*, June 30, 1903) reports a case of laparotomy for severe dysmenorrhœa and menorrhagia in which adhesions confined to the left side of the pelvis had caused a half-turn of the uterus around its long axis from right to left, so that the right adnexa were situated behind the left broad ligament below a cystoma of the left ovary.

A New Method of Preventing Ventral Hernia.—NIKONOW (*Jour. akus. i Shenbolesnej; Zentralblatt für Gynäkologie*, 1904, No. 3) reports a series of cases in which the following procedure was adopted: In opening the abdomen an incision was made about two inches to one side of the median line. After opening the anterior layer of the sheath of the rectus, the muscle is separated by blunt dissection and is drawn outward so that the posterior layer and peritoneum can be incised in the median line.

At the close of the operation the peritoneum and posterior fascial edges are closed separately, then the muscle is replaced and the anterior layers of the fascia and skin are sutured. The writer believes that this is a sure way of preventing subsequent hernia.

Results of Vaginal Hysterectomy for Cancer of the Uterus.—FLAISCHLEN (*Zentralblatt für Gynäkologie*, 1903, No. 52) reports a series of 48 cases in which the cancerous uterus was removed per vaginam. Four patients died from the operation; recurrence occurred in 24. Seventeen were living after an interval of eight years; 12 were free from recurrence after ten years; 9 were well after thirteen years. The writer

contrasts these results with Pozzi's pessimistic statement that out of 204 cases he could report only 2 permanent cures, and believes that his favorable statistics are explained by the fact that in every instance an early diagnosis was made. This supports Winter's statement that the success of the surgical treatment of uterine cancer in the future will depend more on the early recognition of the disease than on the radical nature of the operation, and, in the writer's opinion, proves that radical abdominal hysterectomy will not supplant the vaginal method.

Comparison of Vaginal and Abdominal Hysterectomy for Cancer.—OLSHAUSEN (*Zeitschrift für Geb. u. Gyn.*, Band l., Heft 1) reports 206 vaginal hysterectomies for cancer with 15 deaths, and 4 abdominal with 1 death during the years 1901 and 1902. He prefers the vaginal route until statistics extending over five years shall prove that the results of the abdominal method are better. The fact that Wertheim hopes that from 15 per cent. to 18 per cent. of his cases will be permanently cured by the radical operation does not convince the writer, as his own cures have been 18 per cent.

Conservative Surgery of the Adnexa.—TREUB (*Annal. de gyn. et d'obstétrique*, 1903, No. 5) deprecates hasty resort to a radical operation in cases of adnexal disease, since these rarely result fatally. In 612 cases of salpingo-oöphoritis a more or less complete cure was obtained in 80 per cent. by non-surgical treatment—rest, ice-bags, hot douches and tampons. The mortality after radical operations is from 5 to 6 per cent., and patients are not always relieved of pain, aside from the fact of subsequent climacteric disturbances.

The writer performs posterior section when possible, and when the abdomen is opened always tries to preserve portions of tubes and ovaries, except in cases of tuberculosis, when he extirpates the uterus with the adnexa.

Premature Menopause.—SIREDEY (*Comptes-rend. de la Soc. d'obstétrique de gyn. et de paed.*, December, 1903) reports 5 cases in women whose ages ranged from twenty-two to thirty-five years. Three were in good health; in one menstruation ceased after typhoid fever, though no direct causal relation could be establ shed. One patient subsequently developed diabetes, from which she died. In all menstruation had previously been somewhat scanty, and three had been sterile. Climacteric disturbances were slight. The usual anatomical changes, especially atrophy of the cervix, were well marked. Treatment in true cases of premature menopause is useless.

The Adnexa in Cases of Uterine Fibroids.—DANIEL (*Revue de gyn. et de chir. abdom.*, 1903, No. 1) found pathological changes in 59 per cent. of the cases which he observed. Catarrhal salpingitis was present in one-fourth of the operations, pyosalpinx and pachysalpingitis in others. Hydrosalpinx and hæmatosalpinx, tuberculosis of the tubes, and ectopic gestation were all noted.

The ovaries were more frequently diseased than the tubes (40 per cent.), cystic degeneration, cystoma, and abscess being most common. The writer attributes the adnexal changes to three causes, viz.: 1. Infection. 2. The "fibromatous diathesis," marked by vascular changes

which lead to hyperplasia of fibromuscular tissue. 3. The presence of the uterine fibroids, which causes obstruction in the tubes, with resulting hydrosalpinx or hæmatosalpinx.

Notwithstanding the relative frequency of tubal and ovarian disease accompanying fibroids, this is frequently unrecognized before operation. It should be suspected if the patient complains of pains in the ovarian regions, since these are caused by fibroids only when the latter are impacted. Sterility in women with fibroids is usually due, the writer believes, to disease of the adnexa.

Pyosalpinx Complicating Uterine Fibroids.—STRASSMANN (*Zentralblatt für Gynäkologie*, 1904, No. 4) reports 3 cases (2 of his own and 1 of Lomer) in which pyosalpinx accompanied calcified fibromyomata. He believes that there is a direct causal relation between the two conditions. While the tubes may be infected as the result of septic or gonorrhœal endometritis occurring in a fibroid uterus, pus is rarely found at operations. He infers that prolonged pressure of hard uterine tumors is apt to cause occlusion of the tubes, with the subsequent formation of pus (if bacteria are present) just as occurs in the case of renal calculi.

The Adnexa in Cases of Fibroid.—DANIEL (*Revue de Gynécologie*, Band vii., Heft 2–4) finds that in 207 cases only one-third of the cases of diseased adnexa in connection with fibroid uteri were due to infection. In over one-half there was a diffuse genital "fibromatosis," due to vasomotor or reflex influences. In some cases pressure may be the cause of adnexal disease, as in unilateral hydrosalpinx. The diagnosis is aided by the presence of ovarian disturbances, pressure in the bladder and rectum and symptoms of torsion; 3.68 per cent. of the fatal cases are due to adnexal complications.

Fibroids and Sterility.—AUSTERLITZ (*Prager med. Wochenschrift*, Nos. 23 and 24, 1903) among 339 cases of uterine fibroid found primary sterility in 20.23 per cent. and secondary in 21.25 per cent., as compared with 4.17 per cent. and 13.68 per cent. in women without such neoplasms. The writer was unable to demonstrate whether sterility was directly due to fibroids or not; 51.2 per cent. of women with interstitial tumors were primarily sterile; 22.2 per cent. of the mixed variety; 16.9 per cent. subserous, and 12.7 per cent. submucous.

Appendicitis and Dysmenorrhœa.—MÉRIGOT DE TREIGNY (*Revue prat. d'obstétrique et de gyn.*, 1903, No. 12), in reporting a case illustrating the difficulty of diagnosis between these conditions, quotes from Legendre to the effect that intestinal troubles are apt to be aggravated during menstruation, pain being localized, especially over the appendix. The muscular rigidity characteristic of appendiceal inflammation may be present. The pains sometime cease at once after the discharge of mucus from the bowel. The symptoms simulate those of recurrent rather than acute appendicitis, and the pain is apt to shift from McBurney's point, while the patient's general condition is not such as to suggest the presence of peritonitis.

In the case reported by the writer a girl, aged eighteen years, had severe abdominal pain during menstruation, with obstinate constipa-

t'on. The pains were sometimes localized over the appendiceal region, although they were again equally severe over the left lower abdomen. They were generally relieved by laxatives. As they became intermenstrual and were evidently of intestinal origin, an incision was made over the appendix, which was found to be thickened and adherent. After its removal the pains disappeared; the patient married and had a normal confinement. The writer raises the question whether so-called intermenstrual pain may not often be of appendiceal origin.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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PROFESSOR OF DISEASES OF THE EYE IN THE PHILADELPHIA POLYCLINIC.

Resection of the Cervical Sympathetic Ganglia in Glaucoma.—WILDER, Chicago (*Annals of Ophthalmology*, January, 1904), gives a summary of 68 operations, 7 by himself. Of these operations, 38 were for simple glaucoma, 16 for chronic inflammatory glaucoma, 4 for subacute glaucoma, 3 for acute glaucoma, 4 for absolute glaucoma, 2 for hemorrhagic glaucoma, 1 for buphthalmos; 5 operations were preventive, in none of which has glaucoma occurred. One death occurred. Of the 38 operations for simple glaucoma, 14 gave no improvement whatever, 5 were temporarily improved for periods from fifteen days to eight months, but had recurrent attacks that necessitated iridectomy or caused loss of the eye; 15 were improved as long as they were under observation for periods of from two months to two years. Of these, 3 were stationary, 1 died, 6 remained unimproved after iridectomy, but improved after sympathectomy.

Of the 16 operations for chronic inflammatory glaucoma, 4 were improved, 3 temporarily, 3 remained stationary, and 6 were unimproved. Of the 4 operations for subacute glaucoma, 3 were improved and one temporarily. Of the 3 operations for acute glaucoma, 1 improved, 1 improved temporarily, and 1 remained stationary. Of the 4 cases of absolute glaucoma, 1 was improved, 3 unimproved. Both of the cases of hemorrhagic glaucoma were improved. The case of buphthalmos was improved.

The results in this series of cases do not seem as favorable as those presented by some others; thus Rohner reports 79 improved of 114 operated on. However, there seems a field for this operation, for cases have been reported in which sclerotomy and iridectomy had failed and in which sympathectomy reduced tension and improved vision.

The simple chronic form seems the most suited next to the hemorrhagic. If the operation is to be performed at all Abadie's rule holds:

In acute and subacute glaucoma, iridectomy first; if that fails, sympathectomy; in simple glaucoma myotics twice a day; if in spite of them the vision fails, sympathectomy.

Toxic Amblyopia Caused by Wood (Methyl) Alcohol.—BULLER, Montreal (*Montreal Medical Journal*, January, 1904) reports 3 cases of this lately described affection. The amount taken was about a wineglassful; in the third case three such doses were taken. In cases 1 and 2 the vision was reduced to counting fingers from three to eight feet. In Case 3 the vision was about a quarter of normal and improving. In each of the cases there was, as usual, improvements with quick relapses. In all 3 cases there was evidence of optic atrophy; the third showed only slight pallor of the papillæ.

The pathogenesis of wood alcohol blindness is still a matter of dispute, some holding that the primary lesion is in the retrobulbar portion of the optic nerve and others that it is in the macular region of the retina. Buller considers the optic nerve to be primarily at fault.

Wood alcohol is used in many trades and manufactures, and as even working with materials largely containing it, such as varnish, can induce poisoning from the vapor alone, the public should be informed of the dangers to sight from this substance.

Delirium after Eye Operations.—FINLAY, Havana (*Archives of Ophthalmology*, January, 1904) reports a case of violent delirium following extraction of cataract in a woman sixty-six years of age. Operation of the second eye was followed by nervousness but none of the excitement of the first. Atropine not having been used, could be excluded as the cause, and so could darkness, the patient being in a ward where there was a superabundance of light and air. Alcoholism was not a factor. The twenty-four hours' urine was found to be remarkably scanty and the proportion of urea considerably diminished. Traces of sugar and albumin were also present.

Finlay considers this case as confirmatory of Fromaget's view that such delirium is the result of an autointoxication most often uræmic, in accordance with the views expounded by Regis and Lavaure in 1893 with regard to delirium following operations in general, the source of the intoxication being endogenous or exogenous.

Acute Dacryoadenitis.—INMAN, House Surgeon, Royal London Ophthalmic Hospital (*Reports*, October, 1903), reports 10 cases of this affection observed at the hospital in two years, a rather extraordinary number, considering the experience of others; thus Arlt in his "Lehrbuch," 1853, says he has never seen a case; Powers asserts in 1886 that the indices of the Royal London Ophthalmic Hospital Reports make mention of only one case of abscess of the lacrymal gland. Hirschberg states that among 22,500 recorded cases of diseases of the eye, he met with but one case of suppurative inflammation of the gland.

The cases of this disease described in literature divide themselves into two main groups: (1) Those in which the affection of the lacrymal gland is associated with mumps. The main features are: it is usually bilateral and suppuration does not occur. (2) Those in which there is no connection with mumps, the main features being that it is usually unilateral; suppuration may or may not occur. It is a disease of the

young, although it may occur at all ages. Of the writer's 10 cases—6 males, 4 females—the average was sixteen years, youngest three years, oldest thirty-seven years. The left side was more frequently attacked than the right; thus in this series, 9 out of 10. No cause can be assigned for this marked difference. The connection of this disease with mumps has been noted, though in this series of cases only one was so associated. The lacrymal sac was invariably healthy.

The symptoms are: beginning with a series of sensations of stiffness in the outer part of the upper lid, there is some pain and redness, with slight injection of the conjunctiva. The pain increases with the progress of the disease accompanied by marked œdema of the ocular conjunctiva on the outer side out of all proportion to the conjunctival inflammation accompanying it. The lacrymal gland shows distinct enlargement and induration; the vessels lying upon it are swollen and tortuous; there is moderate malaise and slight fever reaching 100° F. as the highest. As the disease progresses the eye becomes completely closed and the upper lid cannot be raised voluntarily, while eversion of the lid is extremely painful. The disease may be confounded with orbital cellulitis. This probably accounts in part for the rarity of recorded cases.

The outcome is favorable. The treatment is simple, consisting of hot fomentations with free incision to evacuate pus when such can be detected.

OTOLOGY.

UNDER THE CHARGE OF

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The Limits of Variation in the Depth of the Mastoid Antrum.—PHILIP D. KERRISON (*Archives of Otology*, June, 1903) gives some interesting results obtained from making sections of a large number of temporal bones to find out the maximum depth of the antrum to which one can proceed with safety. Politzer gives 15 mm. as a maximum depth, while Schwartze and Broca give 25 mm. and 29 mm., respectively. The author examined thirty bones to discover if any relationship exists between the length of the posterior canal wall and the depth of the antrum. The distance in millimetres between the spine of Henle externally and the inner border of the meatus was measured, then sections through the antrum were made and the distance between the antrum and the mastoid process was taken. In the thirty bones examined the length of the superior canal wall varied from 12 mm. to 18 mm. and in the same bones the depth of the antrum varied from 6 mm. to 15 mm. The deepest antrum measured 15 mm., this extreme depth

occurred in the bone in which the length of the posterior canal wall measured 18 mm. Emphasis is laid upon the fact that the depth of the antrum is invariably less than the length of the posterior canal wall and never exceeds 15 mm.

Broca directs that the antrum be opened in the centre of a square, the anterior border of which is 5 mm. behind the spine of Henle. This point is the thickest part of the mastoid process and naturally the antrum would lie at an unusual depth.

The author also calls attention to the location of the facial and the semicircular canals.

Facial Paralysis.—NORTON L. WILSON (*American Medicine*, vol. vii., No. 7). In addition to its comprehensive review of the subject, this paper contains material of interest to the otologist, both on account of questions of function of the nerve and its branches and of lesions in its course, either secondary to causative conditions in the middle ear or differentiated from them.

The so-called first branch of the facial nerve is the stapedius, supplying the muscle to the stapes; the so-called second branch is a twig to the pneumogastric which, apparently, comes off the facial trunk just above the chorda tympani. This, like the other filaments to the ganglion, is sensory, and undoubtedly goes to the geniculate ganglion, being a part of the *pars intermedia*. The chorda tympani, considered the last branch of the facial in the Fallopian canal, is nothing more nor less than a continuation of the *pars intermedia*, supplying the anterior two-thirds of the tongue with taste. There is, therefore, but one branch in the facial canal which actually comes directly from the nerve, namely, the stapedius, the other branches being all sensory and probably a part of the *pars intermedia*.

In a case of lesion external to the stylomastoid foramen, the paralysis of the facial muscles, including the orbicularis and frontalis, is not associated with disturbances of the senses of taste and hearing.

If the lesion occurs in the lower half of the facial canal, there is, in addition to the facial paralysis, loss of the sense of taste in the anterior two-thirds of the tongue on the affected side and a diminished secretion of saliva, the lesion involving the chorda tympani and twig from the glossopharyngeal nerve.

If the lesion is in the upper half of the canal so that the stapedius is involved and not the ganglion, there is, in addition to the symptoms above named, an abnormal acuteness of hearing, for tones of high pitch especially, because the paralysis of the stapedius permits the unhindered contraction of the tensor tympani, and a correspondingly increased tension of the sound transmitting apparatus of the middle ear.

Concomitant paralysis of the soft palate is usually attributed to involvement of the superficial petrosal, assuming that this nerve comes from the geniculate ganglion. In this opinion the writer does not concur, regarding these filaments as sensory and not motor, and that it is the fifth nerve which innervates the palate, and which is, therefore, the nerve involved when the palate is paralyzed. In support of this contention is the case of a man who fell a distance of eighteen feet, and was picked up unconscious, bleeding from both ears. The hemorrhage from the ears continued for two days, and he was apparently totally deaf, both to sounds aerially conveyed and to the tuning-fork, by bone-con-

duction. The left side of the face was paralyzed, and there was complaint of tinnitus and vertigo. There was a fracture of the base of the skull involving both eighth nerves and the seventh nerve of the left side. There was no sense of taste in the anterior two-thirds of the tongue on the left side, and on this side, also, the salivary secretion was apparently diminished. The uvula and soft palate were normal. Contractility of the muscles of the left side of the face was lost for the faradic current, but was apparently increased for the galvanic current.

Were the geniculate ganglion involved and the general contention correct, the soft palate would have been affected, but in this case it was normal.

Where the cause of a facial paralysis is of otitic origin, attention must be directed to the cause, and the importance of the electric reactions, both as symptoms and as prognostic indications, must be duly regarded. Electric changes soon develop in paralyzed muscles, and the reaction of degeneration, partial or complete, appears in four or five days after the paralysis occurs.

Electricity should not be applied, except to ascertain the excitability of the muscles, until the end of the third week. One month after the paralysis has occurred, electricity and massage should be used regularly and systematically. If the muscles respond to faradism, that current should be used; if they do not, galvanism should be used, but only with the galvanometer, in order that the strength of the current may be known and gradually increased if necessary.

Einige Versuche ueber die Uebertragung von Schallschwingungen auf das Mittelohr.—NAGEL and SAMOYLOFF (*Archiv für Physiologie*, 1898; *Archiv für Ohrenheilkunde*, November, 1903) state that the graphic demonstration of the movements of the drumhead, in response to sound waves or the use of the membrane as a manometric capsule for the same purpose, presuppose some approach to normal flexibility. This is attainable either through the use of fresh specimens or by the infiltration of the tissues of the membrane with substances which serve to conserve its mobility.

For the grosser forms of graphic demonstration, drumheads thus conserved will give good service for a considerable time, months or even years, and may be used also as manometric capsules for demonstration of their movements by actuation of an illuminating gas current feeding a sensitive flame, but never so satisfactorily as the membrane of a freshly killed animal or the normal membrane *in situ* in the living subject.

The latter method consists in making the external auditory canal a closed chamber by means of a stopper having two openings, one by which the illuminating gas enters the canal and the other by which it passes on to the lighted gas jet.

Actuation of the drumhead by singing, speaking, or by communication of sounds conveyed through the bones of the head, are transmitted to the gas current in the external canal and made manifest in the movements of the sensitive flames, care being taken to guard the latter from the extraneous influence of sounds aerially conveyed.

In their experiments Nagel and Samoyloff have used, as a gas chamber, not the external canal, but the tympanic cavity of freshly killed animals and of the living subject. In the former instance the illuminating gas

was introduced by means of a fine trocar passed through the Eustachian tube, while exit to the burner, a platinum tip with a minute opening, was afforded by a drillhole through the thin floor of the tympan and the insertion therein of a small rubber tube. In the living subject a tube with a T-shaped outer end was passed into the Eustachian tube, one end of the "T" connecting with the gas supply, and the other, by means of elastic tubing, with the burner.

Under these conditions sounds conveyed to the drumhead through the external canal and the vocalization of the subject of the experiment, even when only a light whispering voice was used, gave much more detailed representation in the flame than that afforded by the König manometric capsule with a rubber membrane.

Experiments were also made in reference to the question of craniotympanic sound transmission, but, although in themselves interesting, they seemed to have failed to negative the idea of the cranial passage of sound waves direct to the internal ear.

A vibrating tuning-fork, the influence of which upon the flame when held opposite the external canal had been noted, was placed with its stem upon the skull and the character of the flame effect compared with that produced when the external ear was firmly closed, the reaction of the flame, in the latter instance, being much increased.

That the term *craniotympanic*, as referred to the participation of the sound-transmitting mechanism of the middle ear in conveyance to the labyrinth of tones transmitted to the cranial bones is justifiable was shown by another experiment, in which, the vibrating tuning-fork having been placed upon the skull at the point previously found to give the greatest flame reaction, quicksilver or melted paraffin was poured into the external canal, effectively damping the movement of the drumhead. Under these circumstances the craniotympanic reaction was entirely wanting, the sensitive flame showing no movement whatever. On removal of the quicksilver or paraffin the flame immediately responded to the tone of the vibrating tuning-fork.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Measurements of Relative Humidity in Offices and Dwelling-houses in Winter.—An interesting proof of the statement that the air of heated houses in winter surpasses in aridity any climate in the world is given by G. A. LOVELAND (*Engineering News*, December 10, 1903, p. 925), who relates that in consequence of the evident effect of dry air on the furniture in the United States Weather Bureau Office in Lincoln, Nebraska, which is heated by steam radiators, a consecutive record of the relative humidity was made during the following winter. The obser-

vations, made by means of the sling psychrometer, were taken usually twice a day, but sometimes four or five times, and occasionally but once. They showed that during the whole winter the air was exceedingly dry. During the coldest month, February, with a mean temperature of 19.2° F. above zero, the average relative humidity of the office air was but 15.3 per cent. The extreme range was from 7 per cent. to 25 per cent., but only once was the relative humidity higher than 20 per cent., and only once did it fall below 10 per cent. In December, with a mean temperature of 22.6° F., the average relative humidity indoors was 18.6 per cent., and in January, which was the warmest month, with a mean outdoor temperature of 26.8° F., the indoor humidity was 21 per cent. The office temperature during the three months averaged slightly below 70° F. The mean relative humidity outdoors was 77.4 per cent. in December, 73.4 per cent. in January, 77.9 per cent. in February, and 76.2 per cent. for the three months, against but 18.3 per cent. indoors. These results led to further experimentation in a double house, the two halves of which were heated by furnaces of the same size, pattern, and make. The water-pan of each furnace had a capacity of twenty quarts. In one house the amount of water evaporated was determined each day at noon and was found to be but two quarts; in the other the pan was left empty for purposes of comparison. It was found that the difference in relative humidity in the two was so very slight (about 1 per cent.) that the value of the water-pan was not established. After seventeen days' observation the amount evaporated daily was increased to five and nine-tenths quarts by placing pans of water in each of the registers of one house. This resulted in increasing the relative humidity of that house 2.4 per cent. over that of the other. Additional pans were then placed in the cold-air box, whereby the amount of water evaporated daily was increased to ten quarts, but even then the difference in humidity was but 2.2 per cent. Taking into account the probable rate of natural ventilation, it was reckoned that it would require from seventy to one hundred and fifty quarts of water, or possibly more, per day to maintain the relative humidity as high as it was outside, the difference between inside and outside temperatures being from 35° to 50° F., as is the case in winter in Nebraska. In the first period of the experiment the outside and inside relative humidities were, respectively, 68.2 per cent. and 36.2 per cent.; in the second they were 73.8 per cent. and 35.8 per cent.; and in the third, 66.8 per cent. and 29.1 per cent. The average outside and inside temperatures during the three periods were 39.4° F. and 72.1° F., 39.3° F. and 70° F., and 33.3° F. and 69.9° F.

(By means of the "humidifier," which presents to the hot air issuing from a register a surface of wicking kept saturated with water, the relative humidity of the air of a room can be maintained at over 50 per cent., according to Dr. H. J. Barnes, of Boston, who brought it to public notice. In a large office building in Boston the air is maintained at about 50 per cent. relative humidity by means of steam injected into the hot air in the stock-room, from which the air is distributed to the various rooms. The amount of water thus vaporized in a ten-hour workday is no less than 675 gallons.—C. H.)

Shellfish and Typhoid Fever.—It is the belief of Dr. J. T. C. Nash (*Journal of State Medicine*, December, 1903, p. 70) that sewage-con-

taminated shellfish have played a very large if not a leading part in the general incidence of typhoid fever in England. Prior to the advance in sanitary administration, the chief factors in the incidence of the disease were undoubtedly polluted water and infected milk, but to-day these sources have been so attacked that, as compared with fifty years ago, the relative amount of typhoid has diminished considerably. Yet during the past ten years no improvement, but, on the contrary, a tendency to increase, has been observed, in spite of all sanitary effort. No notable instance of epidemic water-borne typhoid has been observed since the Maidstone and Worthing outbreaks, and milk-borne typhoid has been more uncommon; but yet there appears to be an apparently irreducible minimum of typhoid, with an actual slight increase in prevalence. The reason for this is, in his opinion, that sufficient attention has not been given to the consideration of cleanliness of other foods than milk, for otherwise, the mouth being the portal of infection, localities provided with pure water would not have an undue amount of the disease. An infected water-supply causes a widespread epidemic; an infected milk-supply produces the disease among the customers of the particular dairies involved; but when an outbreak occurs where both the water and the milk are above suspicion, there must be some other common source. Polluted soil may be expected to act as a vehicle of infection only by the surface soil becoming pulverized and blown about by the wind, so that it is deposited on articles of food or directly in the open mouth; but surface soil, owing to the action of direct sunlight, dryness, and the ordinary soil bacteria, is not a favorable habitat for the typhoid organism, which, however, finds more favorable conditions in the deeper layers, where there are fewer saprophytes, more moisture, and less light. Yet it must be admitted that aerial infection from polluted surface soil is an occasional factor. On the other hand, contaminated foods are obvious and most probable sources of infection, especially in the case of those which are obtained in polluted water, such as shellfish, water-cress, etc. He believes that a very considerable proportion of cases of typhoid in England is due to sewage-contaminated shellfish, and in substantiation he asserts that out of 105 cases noticed in his district in 1902, he traced some connection with shellfish in at least 82. He cites the fact that at a well-known seaside resort (presumably Brighton) about 30 per cent. of the cases of typhoid that have occurred for some years past have been attributed to this cause, and that at another, where the disease was unduly prevalent in 1898 and 1899 and was attributed to polluted mussels, the stopping of the sale of the mussels the next year was followed by a marked diminution in the number of cases reported. Owing to the bringing about of diminished consumption of shellfish, on the one hand, and of better methods of laying and cooking and of greater care in obtaining supplies from purer layings, on the other, a very decided diminution in the incidence of the disease has occurred in his own district. By careful inquiry, he estimates that rather less than more than 5 per cent. of the population of that district are eaters of shellfish; and working out for typhoid fever the standard ratios during 1902 per thousand persons in each section of the population, he calculates that for the entire population the attack-rate was 3.28 per thousand; for the shellfish-eating section, reckoned as 5 per cent. of the population, it was 51.25; and for the remainder, only 0.75. Among the shellfish vendors and their employés, he cal-

culates the attack-rate at no less than 160 per thousand. Furthermore, the seasonal incidence of typhoid fever in the country generally is at its lowest in May and June, which months are the close season for English and French oysters. During these months, also, cockles and mussels are not in their prime, and hence are less eaten than at other times. In addition to necessary legislation concerning supervision of all shellfish layings and cultivation beds, he recommends for the diminution of the apparently irreducible minimum of typhoid fever the avoidance of all contact with shellfish, except such as are beyond suspicion of sewage pollution, the avoidance of uncooked vegetables which have been subjected to manurial pollution, the early removal to hospital of all cases of the disease, careful and constant attention to effective disposal of sewage and all forms of refuse, and general cleanliness of all food supplies, especially shellfish and watercress.

According to an editorial in the *Journal of the American Medical Association* of January 23, 1904, a careful investigation by the Health Board of Orange, N. J., of a recent increased prevalence of typhoid fever, exonerated the water-supply of the city as the cause thereof, and led to the conclusion that the outbreak was due to the consumption of oysters procured from infected beds.

Concerning Yellow Fever.—Dr. L. O. Howard (Supplement to *Public Health Reports*, November 13, 1903) observes that, although the actual localities in which the *stegomyia fasciata* has been found are comparatively small in number, both in the United States and in other parts of the world, we have sufficient facts on which to base a sound generalization, both as to probable actual occurrence and as to the regions in which the species will readily establish if once introduced. All the occurrence within the United States, except at Nashville, fall within the limits of what are known as the tropical and lower austral zones, which include practically all the southern United States which border on the Atlantic Ocean and the Gulf of Mexico, with the exception of those portions of Virginia, North Carolina, South Carolina, Georgia, and Alabama which constitute practically the foothills of the Appalachian chain, namely, Western Virginia and North Carolina, the extreme northwestern corner of South Carolina, the northern part of Georgia, and the extreme northeastern corner of Alabama. The lower austral zone includes also the western half of Tennessee, the western corner of Kentucky, the extreme southern tip of Illinois, the southeastern corner of Missouri, all of Arkansas except the northern portion, the southern portion of Indian Territory, Southern Arizona, some of Northern Arizona, and southern strips in Utah, Nevada, and California. In the greater part of this territory and where the climate is not too dry, the *stegomyia fasciata* probably exists; and in all the rest of this territory where the climate is not too dry, it will undoubtedly flourish if once introduced. We may expect to find it everywhere in the moist tropical zone, or, at all events, when introduced at any point within the low, moist tropics, it may be expected to establish itself. It is noted that the geographical distribution of the yellow fever mosquito corresponds rather well with that of the Texas cattle tick.

The French Yellow Fever Commission, composed of Marchoux, Salimbeni, and Simond, which has pursued the study of yellow fever at

Rio de Janeiro for more than a year, reports (*Annales de l'Institut Pasteur*, November, 1903) that all the conclusions of Reed and his associates have been confirmed in every particular. Otherwise, its work has been unproductive. DR. G. SANARELLI (*Il Policlinico*, November 21, 1903), however, still opposes the idea that stegomyia is a necessary factor in spreading yellow fever, and asserts anew the importance of the part played by *B. icteroides*.

In a communication to Surgeon-General WALTER WYMAN (*Public Health Reports*, January 15, 1904), under date of December 18, 1903, the members of Working Party No. 2, Dr. M. J. Rosenau, chairman, report that from their studies at Vera Cruz, Mexico, during the summer of 1903, they are unable to corroborate all the findings of Working Party No. 1, having found phases of the organism *myxococcidium stegomyiæ* in normal mosquitoes.

The fact that it has been proved beyond doubt that the female *stegomyia fasciata* serves as an intermediate host and conveys the poison of yellow fever to non-immunes has led the Louisiana State Board of Health to promulgate the following recommendations (*Public Health Reports*, February 5, 1904): 1. The patient shall be put under a bar and the room properly screened, and all mosquitoes destroyed. 2. The house shall at once be closed and fumigated with pyrethrum powder, 4 ounces to 1000 cubic feet. Intoxicated mosquitoes must be swept up and burned. In case house is not occupied, sulphur should be used, 7 pounds to room, etc. Fumigation must be repeated every fourth day for three or four times. Commence all over with every new case of fever. 3. Every house or outhouse shall be so fumigated for a distance of 100 yards in every direction from the infected house. Fumigation repeated every fourth day for three or four times. 4. Great care to be exercised to prevent new mosquitoes from entering the infected room. When they do so, they must be killed and burned. 5. All cisterns in infected area must be screened or coal-oiled. 6. All vessels containing water must be emptied; pools and ditches drained and coal-oiled. 7. All drains, sinks, and privies are to be liberally sprinkled with coal-oil every third day for a period of eighteen days. Repeat after every new case.

PATHOLOGY AND BACTERIOLOGY.

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A Note on Experimental Arterial Atheroma.—Attempts have been made by several investigators to produce atheroma of the aorta in animals by intravenous injections of bacteria or bacterial toxins. In some cases the aorta was previously injured. Crocq has reported nega-

tive results, while Thérèse and Pernice were only able to produce very slight microscopic lesions in the wall of the aorta. Boinet and Romary have described small, raised areas in the aorta, which, on microscopic examination, had the characters of gelatiniform plaques. They believed these areas were the result of bacterial infection of the arterial wall. Josué has observed the formation of true calcareous plates after repeated injections of adrenalin. GILBERT and LION (*Arch. de méd. exp. et d'anat. path.*, 1904, T. xvi. p. 73) describe lesions in the aorta which they found in two rabbits after repeated intravenous inoculations of both living and killed cultures of a paracolon bacillus. In these experiments the artery did not receive any previous injury. One animal was allowed to live six months, the other ten months, after the primary inoculation. The middle coat of the aorta was the one affected, and the lesion consisted in a sclerocalcareous transformation. In another series of experiments the aorta was injured, and later cultures of typhoid bacilli were inoculated intravenously. After a few days the animals were killed. An acute aortitis was found at the site of trauma. The authors conclude that it is possible to produce atheroma of the aorta and acute aortitis in animals by intravenous inoculations of bacteria and bacterial toxins. This may take place with or without previous injury to the arterial wall.

Scarlet Fever, Protozoan-like Bodies Found in Four Cases.—MALLORY (*Journal of Medical Research*, 1903, vol. x. p. 483) has found in four cases of scarlet fever certain bodies which in their morphology strongly suggest that they may be various stages in the developmental cycle of a protozoan. They occur in and between the epithelial cells of the epidermis and free in the superficial lymph vessels and spaces of the corium. The great majority of the bodies vary from 2 to 7 microns in diameter, and stain delicately but sharply with methylene blue. They form a series of bodies, including the formation of definite rosettes with numerous segments, which are closely analogous to the series seen in the asexual development (schizogonia) of the malarial parasite, but, in addition, there are certain coarsely reticulated forms which may represent stages in sporogonia, or be due to degeneration of other forms. The bodies were not found in the blood, lymph nodes, or any of the internal organs. The possibility of these bodies being artefacts or degenerations can be effectually excluded. If they are protozoa they must have some causal relation to scarlet fever, for were they normal or occasional inhabitants of the skin, their presence could hardly have been overlooked in he extensive work which has been done on the skin. Though the author believes that these bodies are protozoa and have an etiological relationship to scarlet fever, he does not claim that such a relationship has been absolutely proven. He proposes the name of "cyclaster scarlatinalis" for the organism.

Tuberculosis of the Tonsils in Children.—The belief has steadily been gaining ground that the tonsils are one of the most important channels by which the tubercle bacillus enters the system during childhood. A comparatively large number of cases in which tubercle bacilli or tubercles could be demonstrated in the tonsils of adults have been recorded, but only a few observers, especially Friedmann and Latham, have confined their attention to the study of the tonsils in children. KINGSFORD (*Lancet*, 1904, vol. i. p. 89) has examined the tonsils of seventeen

children under five years of age, which at autopsy showed tuberculous lesions in various parts of the body. Tuberculosis of the tonsils could be demonstrated microscopically in seven of these cases, but in only one was there any evidence that the tonsillar infection was primary. In the other cases the infection probably took place by means of the blood stream or expectorated sputum. The author concludes that though tuberculosis of the tonsils is fairly common, the process is rarely primary in the tonsils. If the tonsils are tuberculous the cervical glands are also affected, but it may happen that the infection enters the body through the tonsils and reaches the cervical glands without leaving a demonstrable lesion in the tonsils themselves.

The Pathological Anatomy of "Paratyphoid Fever:" Report of a Fatal Case with Bacteriological Findings.—WELLS and SCOTT (*Journal of Infectious Diseases*, 1904, vol. i. p. 72) have collected the pathological and bacteriological reports of four fatal cases of paratyphoid fever. They describe in detail the history, bacteriology, and pathological findings of a fifth case. The case was one simulating typhoid fever, but giving negative Widal reactions throughout the course. The spleen was palpable, rose spots were present over the abdomen, and twice blood was passed in the stools. There was absence of depression, little or no delirium, and a relatively high pulse rate. At autopsy the general pathological picture was that of an acute infection. In the ileum, a short distance above the ileocæcal valve, an extensive ragged ulceration was found; the ulcers bore no relation to the lymphatic apparatus and appeared entirely dissimilar to the ulceration of typhoid fever, inasmuch as they were quite superficial and showed lack of infiltration. They resembled much more the ulcers of dysentery. There was no swelling either of the mesenteric or retroperitoneal lymph nodes. In sections the ulcers in the ileum looked entirely different from typhoid ulcers, particularly in the absence of infiltration and hyperplasia of the lymphoid follicles. The mesenteric lymph glands also showed total absence of congestion or lymphoid swelling of the lymph follicles and sinuses. A few foci of necrosis were seen in the liver. They were noticeable for their lack of endothelial cells. The spleen showed congestion with the presence of large endothelial cells containing golden-brown pigment. Cultures from the spleen and kidney gave a pure growth of paratyphoid bacilli. With the serum of a rabbit immunized against Buxton's paratyphoid bacillus, they agglutinated in dilutions of 1: 40,000. The serum did not react toward typhoid or colon bacilli. The authors conclude that paratyphoid infections are accompanied by changes quite different from those of typhoid fever. The intestinal lesions are variable, and there is little anatomically to differentiate this type of infections from other septicæmias.

Influence of Splenectomy on the Leukocytes of the Blood of the Dog.—NICOLAS and DUMOULIN (*Jour. de phys. et de path. gén.*, 1903, T. v. p. 1073) conclude, from a study of the blood in two splenectomized dogs, that after splenectomy there is an increase in the number of white blood cells, and that this increase persists for some time after the operation, but eventually, perhaps after months, returns to the normal. There is an immediate diminution in the number of leukocytes, followed by a transient elevation of these cells. This finally gives place to a marked

and persistent decrease in the relative number of lymphocytes. The authors believe that this observation is important, inasmuch as it suggests that the spleen plays some part in the genesis of the lymphocytes. The polymorphonuclear leukocytes show a slight variation and are usually relatively increased. A marked eosinophilia occurred in one of the two dogs.

Changes in the Power of Absorption of the Animal Peritoneum Brought about by Intraperitoneal Injections of Adrenalin.—It is well known that the application of adrenalin to mucous surfaces causes anæmia, owing to the contraction of the capillaries. EXNER (*Zeitschrift für Heilkunde*, 1903, Bd. xxiv. p. 302), applying this principle to serous surfaces, experimented with adrenalin to study its effect when, injected intraperitoneally, upon the absorbing power of the peritoneum. Guinea-pigs and rabbits received intraperitoneal injections of adrenalin. Subsequently, when strychnine, potassium cyanide, physostigmine, and indigo were given into the peritoneum, the onset of toxic symptoms from these drugs or their absorption was much delayed over the control animals. With potassium iodide, the time required for its appearance in the urine was the same in normal animals and animals which had received adrenalin intraperitoneally. To determine whether the adrenalin injections affected the absorption through the bloodvessels or lymphatics, a fine emulsion of paraffin in gum arabic was used. The absorption of this substance was much retarded by previous intraperitoneal injections of adrenalin. By staining the diaphragm with silver nitrate, the structures described as stomata appeared less numerous in the adrenalin animals than in the normal animals. It was, therefore, thought that absorption through the lymphatics alone was retarded by adrenalin. Adrenalin injections had a very marked retarding effect upon the extension of bacteria from the peritoneum into the circulating blood.

From the results of these experiments, the author suggests that in operations for peritonitis a very material benefit might be derived by previously injecting adrenalin into the peritoneal cavity. By this procedure it is possible that the absorption of bacterial toxins from the peritoneum might be lessened during the manipulation of the intestines at operation.

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